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BULLETIN

OF THE NEW YORK ACADEMY OF MEDICINE

Original Articles

by

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REPORT ON DRUG ADDICTION
COMMITTEE ON PUBLIC HEALTH

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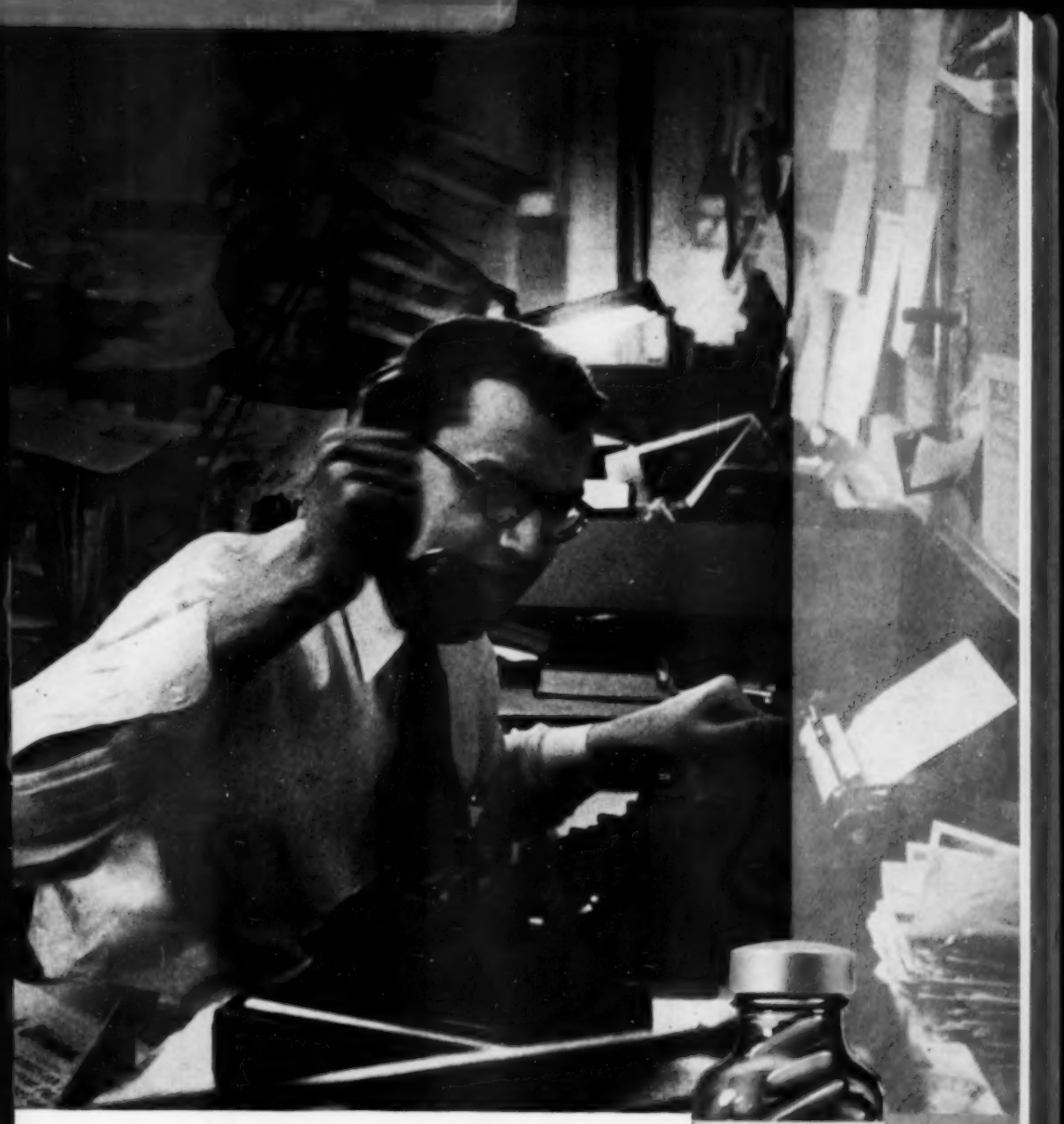

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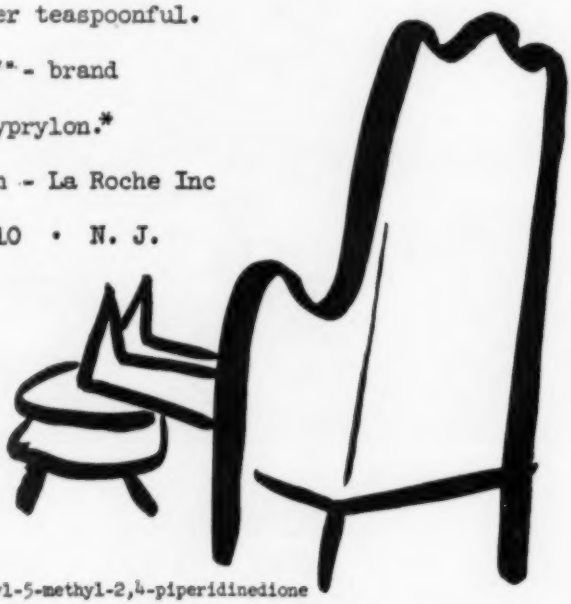

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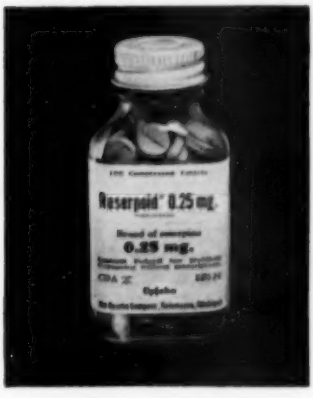

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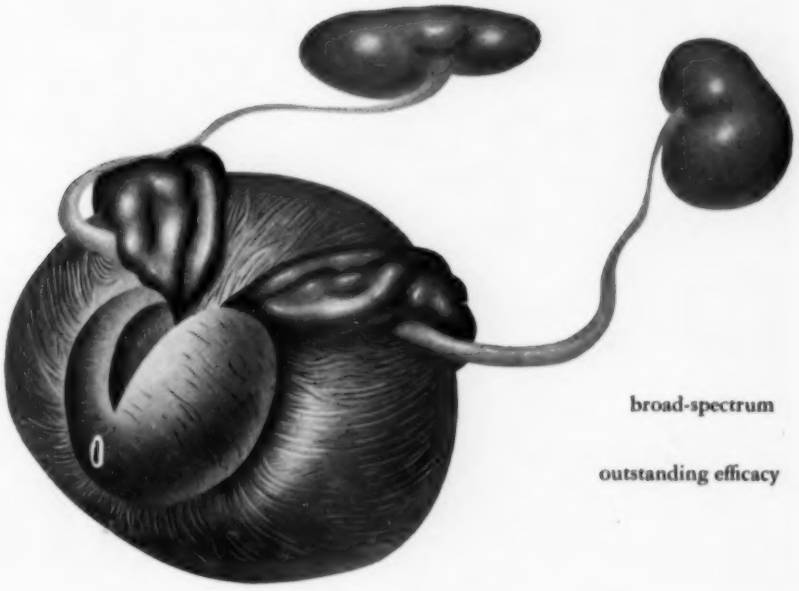

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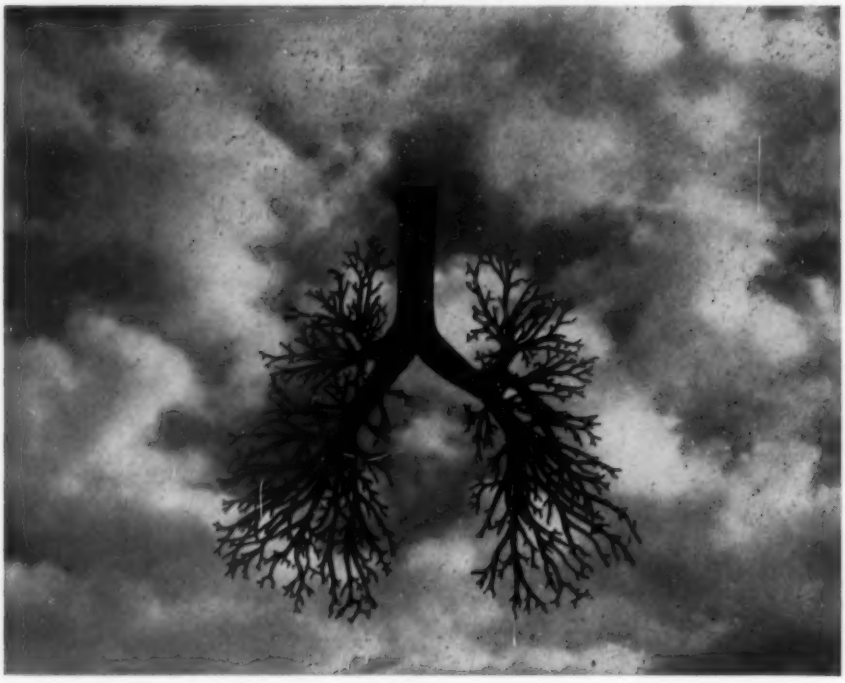

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Subcommittee on Drug Addiction

AUTHORS ALONE ARE RESPONSIBLE FOR OPINIONS EXPRESSED IN THEIR CONTRIBUTIONS

ROBERT L. CRAIG, *Editor*

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BULLETIN OF
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VOL. 31, NO. 8 AUGUST 1955

A CURRENT VIEW ON THE PROBLEM OF DRUG RESISTANT STAPHYLOCOCCI AND STAPHYLOCOCCAL INFECTION*

VERNON KNIGHT and HARVEY S. COLLINS

THE enormous increase in the resistance of staphylococci to antibiotics has raised two important questions for clinicians. The first is concerned with understanding the factors which control the development and distribution of drug resistant staphylococci in man. The second is that of evaluating the effect of drug resistance on human staphylococcal infections.

The questions are important to physicians because drug resistance of staphylococci is undoubtedly a consequence of the use of antibiotics in the treatment of infections. Furthermore, based on studies of the mechanism of development of drug resistance of staphylococci, it appears that more orderly regimens of antimicrobial therapy might permit some control of patterns of antimicrobial resistance of staphylococci.

The earliest reports of drug resistance of staphylococci were con-

* Presented by Dr. Knight at the 27th Graduate Fortnight of The New York Academy of Medicine, October 26, 1954.

From the George Hunter Laboratory, Department of Medicine, Vanderbilt University Medical School, Nashville, Tenn. (Dr. Knight), and the Division of Clinical Investigation, Sloan-Kettering Institute, and Departments of Medicine and Bacteriology, Memorial Center, New York City (Dr. Collins).

cerned with cultures which were distinguishable from each other only by differences in drug susceptibility. More recently, however, the method of identification of individual strains of staphylococci by phage typing has been used. Although the procedure at present is not ideal, it offers important information to supplement other means of differentiating among the staphylococci. In 1953 and 1954 this procedure was employed in a study of staphylococci at Bellevue Hospital[1] and at Memorial Center.[2] In a subsequent part of this report data illustrating its benefits will be described.

When the increasing extent of resistance of staphylococci to antimicrobial drugs first was appreciated it was anticipated that this would result in serious problems in the treatment of staphylococcal infections. While admitting that resistant organisms in an infection present a serious impediment to effective therapy, we believe that this factor is only one of several which affect the outcome of staphylococcal infections and at present plays a disproportionately smaller role than the great magnitude of the phenomenon of drug resistance of staphylococci in our hospitals would suggest.

In the present report we have chosen therefore, to discuss the drug resistance of human staphylococcal flora and to attempt to analyze the influence of drug resistant staphylococci in human infection.

Increasing Resistance of Staphylococci to Penicillin and Other Agents

In Table I are described published reports which illustrate the great increase in the occurrence of penicillin-resistant staphylococci following the introduction of this agent into clinical use. For example, Spink in Minneapolis[3] found only 12 per cent of 68 strains of staphylococci which showed resistance to penicillin in 1945 and in most this was slight in degree. In succeeding years there was a regular increase in resistance of staphylococci in hospitals in widely separated areas of the world. The regular increments of resistant strains in each succeeding year, despite the divergent source of the reports is especially interesting. The highest percentage of resistance observed was 88 per cent in a report by Dowling from Chicago in 1951.[4]

In contrast to hospitals, carrier rates of resistant staphylococci in the general population have only slowly increased, ranging only from less than 10 per cent to 32 per cent in the period 1948 to 1951. The

TABLE I—INCREASING RESISTANCE OF STAPHYLOCOCCI TO PENICILLIN

Year Isolated	Location	Hospital Patients		Non-hospitalized carriers		References
		No. strains	Per cent resistant	No. strains	Per cent resistant	
1945	Minneapolis	68	12 (slight in degree)			Spink[5]
1946	London	200	12.5			Barber[53]
1946-7	Bergen	287	18.8			Bøe, *et al.*[39]
1947	London	100	38			Barber[53]
1948	London			315	7.6	Voureka, *et al.*[54]
1948	London	100	59			Barber, *et al.*[55]
1948-9	Sydney	228	53	90	8.8	Rountree, *et al.*[56]
1949	Bergen			1304	3.9	Vogelsang[57]
1949	London	38	68.4	40	12.5	Forbes[58]
1949	Oxford	426	50	568	24	Summers[59]
1950	Minneapolis	104	55.8			Spink[5]
1951	Chicago	42	88	84	32	Dowling, *et al.*[4]
1951-2	Boston	500	73			Finland[6]

fact that values from the general population are frequently lower than the earliest reported values from hospitals suggests that even in 1945, hospital staphylococci had felt the influence of penicillin. At Bellevue Hospital in 1953-54 a survey of drug resistant staphylococci was made and for comparison 55 strains which were obtained from patients at Postgraduate Hospital in the period 1932-48 were available.[1] These two groups in point of time of isolation fit at the extremes of Table I, and the values for penicillin resistance are consistent with those reported in the table. For example (Table II), in the period 1932-48, largely before penicillin was available, only 7 per cent were resistant, and at Bellevue Hospital in 1953-54, 72 per cent were resistant. It was observed that a majority of the few penicillin resistant strains in the earlier collection were isolated after penicillin was widely used.

The introduction of chlortetracycline and oxytetracycline was soon followed by the appearance of increasing numbers of staphylococci resistant to them. In 1950 Spink[5] found only 4.8 per cent of strains from hospital patients were resistant to these agents whereas Dowling,[4] in a small series in Chicago in 1951, found 78 per cent of hospital strains were resistant. Among strains from non-hospitalized carriers in Chicago in 1951, however, only 4 per cent were resistant. Finland[6] found 23.6 per cent of 500 strains isolated at Boston City Hospital in 1951 and 1952

TABLE II—SUSCEPTIBILITY OF STAPHYLOCOCCUS AUREUS TO ANTIBIOTICS

1932-48	Postgraduate Hospital	55 strains
1953-54	Bellevue Hospital	516 strains

		Sensitive per cent	*Intermediate per cent*	*Resistant per cent*
penicillin	Postgrad.	78	15	7
	Bell.	15	13	72
tetracyclines	Postgrad.	100	—	—
	Bell.	33	1	66
streptomycin	Postgrad.	4	92	4
	Bell.	1	33	66
erythromycin	Postgrad.	89	11	—
	Bell.	97	2	1
chloramphenicol	Postgrad.	2	94	4
	Bell.	5	86	9

Condensed from Knight and Holzer, J. clin. Invest.[1]

were resistant to chlortetracycline and 32.2 per cent were resistant to oxytetracycline.

In our studies in New York[1] 66 per cent of strains from Bellevue Hospital which were collected in 1953-54, were resistant to the tetracyclines while none of the 55 strains collected at Postgraduate Hospital before these agents were available were resistant to the tetracycline drugs.

Resistance of staphylococci to streptomycin increased in a similar manner to penicillin except that streptomycin was never highly active against staphylococci, with 92 per cent of the 55 strains isolated in 1932-48 falling into an intermediate range of susceptibility (6-50 mcg/ml.). At Bellevue in 1953-54 resistance of staphylococci to streptomycin was found in 66 per cent of 516 strains. These findings are in agreement with observations by Spink[5] and others.[6]

A majority of both New York City collections were sensitive to erythromycin and the few strains in the intermediate range fell into the lowest category (inhibited by 6 mcg/ml., not by 3 mcg/ml.). A few resistant strains in the Bellevue Hospital collection were isolated from patients who had been treated with erythromycin.

Chloramphenicol was apparently never highly active against staphylococci, but the strains collected in 1953-54 showed no appreciable

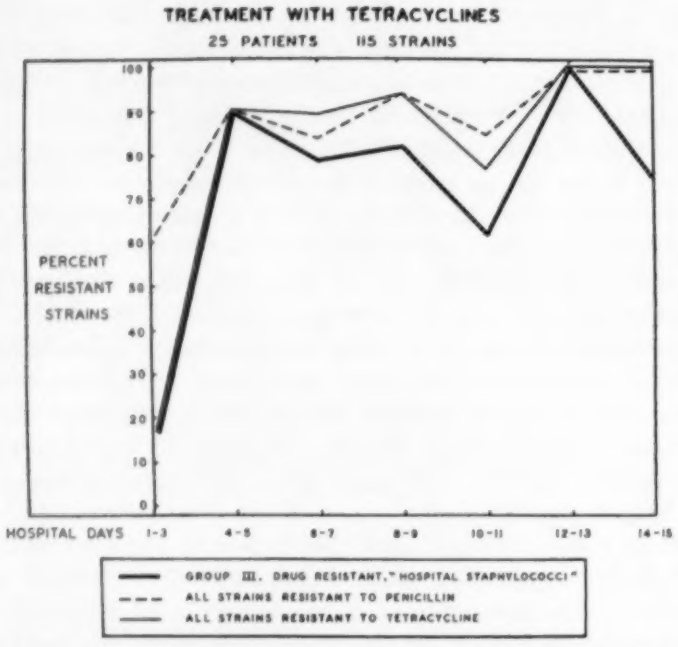
increase in resistance to this agent. This is in agreement with Spink's studies in Minneapolis[5] and of Needham and Nichols at Mayo Clinic.[7] Although it is true that this drug was not so widely used as the other agents in recent years, it is by no means certain that lack of exposure of staphylococci to it explains the lack of increasing resistance.

In an effort to determine the extent to which staphylococci were resistant to the various agents in the general population, resistance of strains which were cultured during the first of seventy-two hours in the hospital were examined (strains presumed to have been brought to the hospital). It was found that 62.7 per cent of 67 strains were resistant to penicillin but only 13.4 per cent were resistant to the tetracyclines. Streptomycin resistance was almost identical with penicillin resistance. A certain amount of admixture of these strains with strains acquired in the hospital seemed probable, but the low values for tetracycline resistance suggested that it was not very great. It seemed reasonable to conclude, therefore, that these values were representative of the non-hospital population of a section of the Metropolitan area.

Phage Types of Drug Resistant Staphylococci: The staphylococci in the New York studies just described were subjected to the phage typing procedure.[8] The great majority of strains were lysed by one or more of the test phages, which permitted their classification into one of three large groups of staphylococci. Since these groups have been found to correspond to Cowan's serologic groups I, II, and III, these designations are used for identifying the appropriate phage type groups.

The principle findings resulting from the use of this procedure at Bellevue was related to the strains of staphylococci which were resistant to the four antibiotics, penicillin, streptomycin, chlortetracycline, and oxytetracycline. These strains numbered 338, two-thirds of the total of 516 isolated in 1953-54 at Bellevue; of these 338 multiple drug resistant strains, it was found that virtually every one fell into phage group III, and that a great majority were lysed by combinations of three different group III phages 6, 47, VA4.

From the total group of 516 strains were separated all those which had been isolated from patients during the first seventy-two hours in the hospital, strains which were presumed to have been brought into the hospital by the patients. In contrast to the results above, it was found that only 13.4 per cent were resistant to the four antibiotics and were of group III phage patterns. Correlated with these observations was the



* Figure 1. Strains indigenous to the hospital, characterized by resistance to penicillin, streptomycin, the tetracyclines and of group III phage types increased from a low percentage to near 100 per cent by the 4- to 5-day period and remained high thereafter. On admission about 60 per cent of strains were resistant to penicillin, most of which were not "hospital staphylococci." Later penicillin resistance was chiefly accounted for by "hospital staphylococci." (From Knight and Holzer, J. clin. Invest.[1])

finding of Collins[2] at Memorial Center that only 23 per cent of a series of outpatient cultures of staphylococci were of group III phage patterns.

Thus was demonstrated that a high predominance of phage group III staphylococci resistant to multiple antibiotics was characteristic of the hospital patients, but probably not of the flora of non-hospitalized persons in that area.

Effect of Antimicrobial Therapy and Hospitalization on the Acquisition by New Patients of Staphylococci Indigenous to the Hospital: In 1950 Cairns and Summers[9] reported that the proportion of penicillin-resistant staphylococci carried by patients increased as the length of

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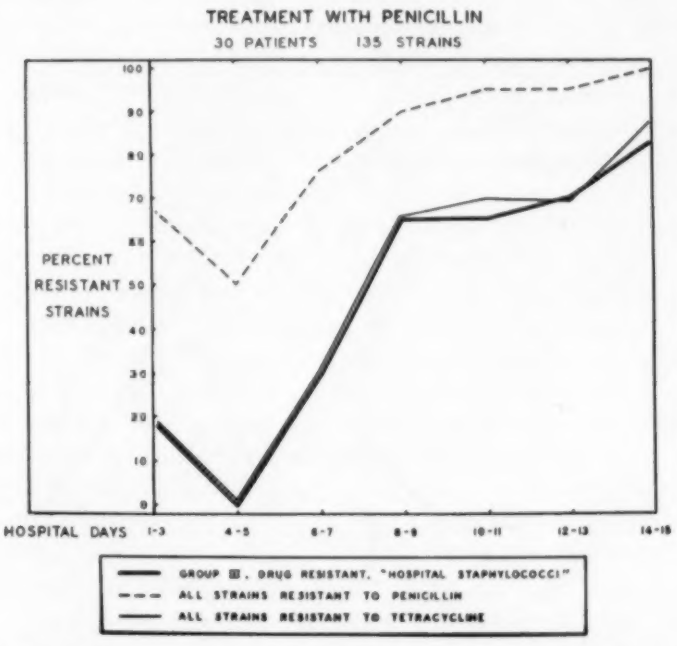

Figure 2. Strains indigenous to the hospital (heavy line) increased in per cent less rapidly in these patients than in the group treated with tetracyclines, but during the second week reached high values. The curve of penicillin resistance was similar to that of patients treated with tetracyclines, except that it did not increase as rapidly as among those patients. (From Knight and Holzer, J. clin. Invest.[1])

their stay in the hospital increased. This general problem was considered in the Bellevue study by determining the rate at which the staphylococci resistant to multiple antibiotics and of group III phage types appeared in cultures from patients on two different regimens of antimicrobial therapy, and in others who received no treatment.

The results of this study indicate that antimicrobial therapy may influence the rate of acquisition of these resistant "hospital staphylococci" of group III phage types. For example, among patients treated with tetracyclines (Figure 1) there was a very rapid increase in the proportion of resistant "hospital staphylococci" from less than 20 per cent in the one- to three-day period to values near 100 per cent by the four- to five-day period and thereafter. Patients treated with penicillin

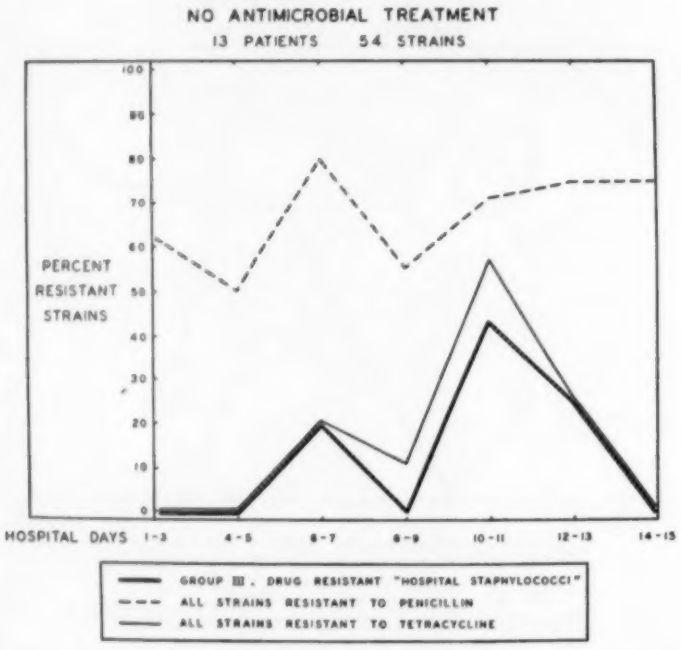

Figure 3. Patients receiving no antimicrobial treatment acquired "hospital staphylococci" more slowly than the two treated groups. Penicillin resistance was about 60 per cent on admission and increased only slightly during hospitalization. This reflects the failure to acquire penicillin resistant staphylococci from the hospital reservoir ("hospital staphylococci"). (From Knight and Holzer, J. clin. Invest.[3])

(Figure 2), and some who also received streptomycin, showed a less rapid increase in the per cent of resistant "hospital staphylococci." Values did not exceed 30 per cent during the first week although they rose to near 100 per cent thereafter.

Patients who received no antimicrobial treatment (Figure 3) showed only sporadic elevations in the percentage of resistant "hospital staphylococci" during two weeks of observation. Statistical analysis revealed that the degree of increase in the percentage of "hospital staphylococci" in the three groups of patients was significantly different and the interpretation is offered that the differences are a result of antimicrobial therapy.

They appear to be explained in the following way. On admission only a small percentage of strains was resistant to the tetracycline derivatives. Treatment with this agent could be expected to inhibit the large majority of sensitive strains, and provide an opportunity for the tetracycline-resistant strains in the hospital to establish themselves in these patients. Since admission cultures yielded slightly more than one-half of strains resistant to penicillin, use of this agent had less effect on staphylococci brought to the hospital than did tetracyclines and less opportunity was offered for "hospital staphylococci" to replace strains carried on admission. Patients receiving no treatment had no reason to lose staphylococci, whether resistant or sensitive, and thus provided the least opportunity for "hospital staphylococci" to be acquired.

There is evidence from a number of other sources that a great majority of antibiotic resistant staphylococci are in phage group III[10-14] and that among drug susceptible staphylococci there is a much more nearly equal distribution of strains among the three phage groups.[10, 13] Since antibiotics are used most intensively in hospitals, these centers are foci of the highest concentration of drug resistant staphylococci and consequently of strains of group III phage patterns. Furthermore, evidence suggesting that phage group III staphylococci did not always predominate among staphylococci in hospitals was obtained when it was found that only 20 per cent of the very largely drug susceptible strains collected at Postgraduate Hospital in the period 1932-48 were in phage group III.[1]

There is no explanation at present for this linkage between resistance to antimicrobial drugs and lysis by group III phages, and it may be a unique example of the association of certain biological characteristics within a bacterial species with the capacity to become resistant to antimicrobial drugs.

Infection with Drug Resistant Staphylococci

In an earlier section of this report the opinion was expressed that the results of the present day treatment of staphylococcal infections, many of which are caused by drug resistant strains, are about as good as they were during the early penicillin period. Statistically sound evidence concerning any aspect of staphylococcal infection is difficult to obtain, but from published reports and our own observations, data will be presented (p. 559) which suggest that the recent overall mortality from

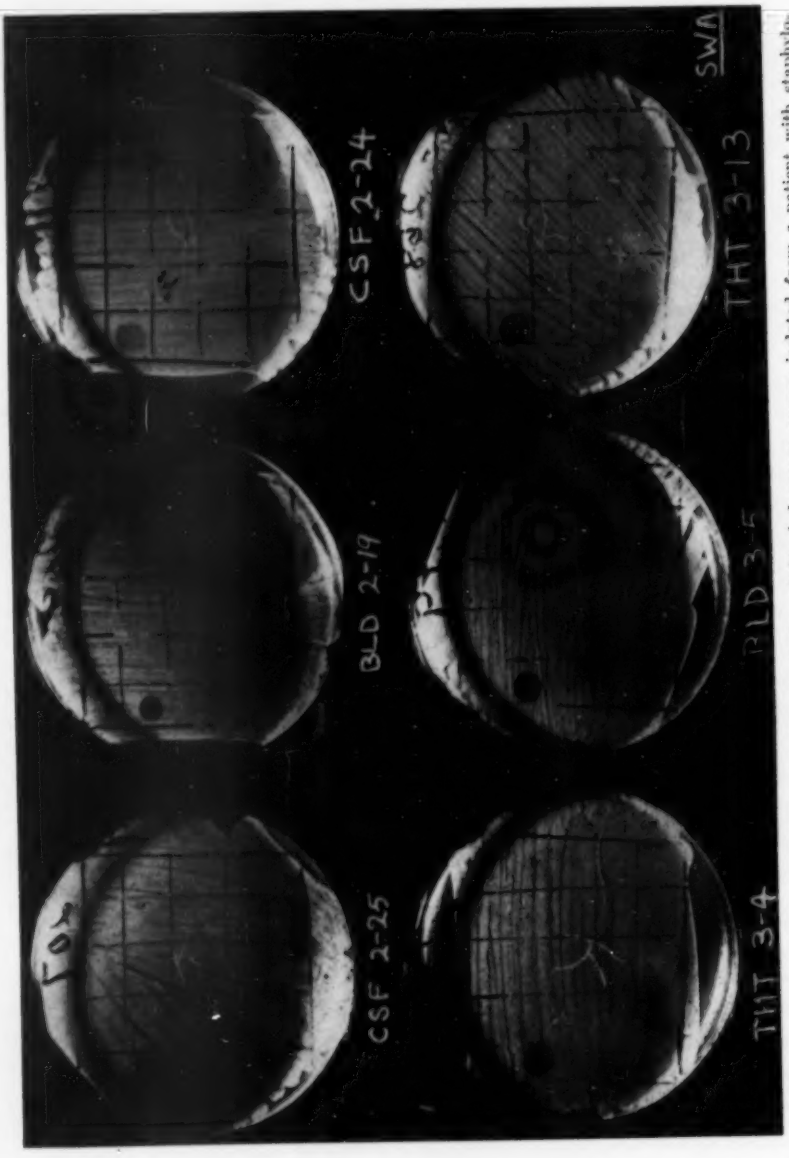

Figure 4. Photograph of phage typing of 6 of 44 strains of Staphylococcus aureus isolated from a patient with staphylococcus meningitis and bacteremia. Strains of identical phage types were cultured from spinal fluid, blood, nose, throat and rectum during the patient's illness.

acute, generalized staphylococcal infection is no higher than it has been at various times since penicillin was introduced into use, and that it is somewhat lower than it was in the pre-penicillin period.

Mortality from Staphylococcal Bacteremia before and after the Introduction of Antibiotic Therapy: When untreated the mortality rate of staphylococcal infection associated with bacteremia is very high. In the seven year period before 1941, Skinner and Keefer[15] found that the mortality rate for 122 cases admitted to the Boston City Hospital was 81 per cent. MacNeal, Frisbee, and McRae[16] reported only 165 survivors out of 500 cases (33 per cent) of staphylococcal bacteremia in a study of the therapeutic effect of staphylococcal bacteriophage at Postgraduate Hospital in New York in the period 1931 to 1940.

No large studies are available for comparison in the early period of penicillin therapy but Wise and Spink have reported a mortality rate of 28 per cent of fifty-seven cases treated in Minneapolis.[17] Of this number twenty-eight were bacteremic and it seems probable that the survival rate would be somewhat lower if limited to these cases only.

Dowling and Lepper[18] and their associates have reported that of seventy-six cases of staphylococcal endocarditis collected over a period of several years in which antibiotics, principally penicillin, were used, the mortality rate was 53 per cent.

Several reasons can be advanced to explain the high mortality of staphylococcal infection. Important among them is the fact that the disease very often occurs in patients with diabetes, arteriosclerosis, neoplastic disease, or other debilitating illness. Second, that if the disease is not checked early in its course metastatic abscesses may form which are difficult to locate or are so widely distributed that they are impossible to treat effectively.

In any event it is apparent from these reports that although the mortality rate of staphylococcal infection was reduced somewhat by penicillin treatment, there remained a substantial percentage of fatal cases. Although some mortality might be attributable to drug resistance of infecting strains, the occurrence of fatalities in cases with penicillin susceptible infections and the survival of others with strains resistant to penicillin suggest that other factors are important in influencing the mortality rate.

There are fewer recent studies of the treatment of staphylococcal infections with the newer antibiotics but Wise and Spink[17] have reported

TABLE III—CHARACTERISTICS OF STAPHYLOCOCCUS AUREUS FROM PATIENTS WITH INFECTION

Patient	*Location of infection*	*Antibiotic treatment*	*Result*	*Phage type*	*Drug susceptibility* tetracyclines mcg/ml	penicillin mcg/ml
Ha.	Bacteremia Empyema	Penicillin Streptomycin	Recovery	47 VA4, Grp. III (Blood 1,* Pl. fluid 2,4) 6 47, Grp. III (Pl. fluid 3, 10)	3 >50	0.1 0.1
Pa.	Bacteremia Meningitis Pyodermia	Penicillin Streptomycin Carbomycin	Recovery	42b 47c, Unclass. (Blood 6) 3b, Grp. I (Blood 8)	3 >50	0.1 25
Mi.	Endocarditis	Penicillin Streptomycin Terramycin	Recovery	44a, Grp. I (Blood 1, 5, 14) No type (Blood 28, 42, 45)	Sensitive Resistant	Sensitive Sensitive
Ma.	Bacteremia Lung abscess	Penicillin Streptomycin Chlortetracycline Erythromycin	Recovery	47, Grp. III (Blood)	>50	25
Sw.	Bacteremia Meningitis	Penicillin Streptomycin Chloramphenicol Chlortetracycline Erythromycin	Recovery	47, Grp. III (Blood, C S F, see text)	>50	25
Du.	Bacteremia	Penicillin Streptomycin Oxytetracycline	Recovery	6 47, Grp. III (Blood)**	Resistant	Resistant
Do.	Bacteremia	Penicillin Streptomycin Chloramphenicol Erythromycin	Death	6 47, Grp. III (Blood)**	Resistant	Resistant
Gr.	Bacteremia	Penicillin Streptomycin Carbomycin	Death	47 VA4, Grp. III (Blood)	>50	25

* Hospital day strain isolated

**These two patients from Memorial Hospital

a mortality rate of 54 per cent in twenty-two cases treated at the University of Minnesota Hospitals. Descriptions of their cases indicate that there was a very high proportion of complicating illnesses, including neoplasms in eight of the cases and other important surgical or medical diseases in nine others. In all but one of the twelve fatal cases at least four antibiotics, usually including erythromycin, were used in high dosage, and strains from all patients were reported to be susceptible to this agent.

It is possible that had these patients had infections with penicillin susceptible organisms, penicillin treatment might have affected their course more favorably than erythromycin did under similar circumstances. Judging from the evident severity of these cases, however, it seems more likely that many of them are further examples of the overwhelmingly severe nature of staphylococcal infection in which even optimum antimicrobial therapy may not be of benefit.

During the greater part of 1953 and 1954 while the survey of carriers described earlier in this report was underway, special study was made of cases of staphylococcal infections which occurred on the Cornell Medical Division at Bellevue. During this interval five cases of staphylococcal bacteremia were encountered. In addition three cases from two other institutions were observed. In five of the eight cases the infection was caused by drug resistant staphylococci and in three it was caused by strains susceptible to penicillin and the tetracyclines (Table III). All of the drug resistant strains were of phage group III, while the drug susceptible strains were respectively in phage group I, III, and unclassifiable. Strains from all eight patients were highly susceptible to erythromycin.

The three patients with drug susceptible infections recovered as did three of the five with drug resistant infections. The mortality rate of the five cases with resistant infections, therefore, was 40 per cent and of the total series of eight was 25 per cent. One of the patients who died was treated with erythromycin without effect. Both of the patients with fatal infections were critically ill and recovery seemed doubtful at the time treatment was begun. One had carcinoma of the breast with metastases and death occurred following hypophysectomy for palliation. In the other an abdominal malignancy was suspected although permission for autopsy was not obtained. Since most cases at present, in our experience, are caused by "drug-resistant staphylococci" it is probable that

TABLE IV—SUMMARY OF A CASE OF STAPHYLOCOCCUS AUREUS BACTEREMIA AND MENINGITIS

	Course	Treatment	Cultures for Staphylococcus aureus: Site	No. strains	Phage pattern	Susceptibility to: penicillin	tetracyclines	streptomycin	erythromycin
Feb. 1953	critically ill	chlortetracycline	Blood	7	47	R*	R	R	S**
		Carbomycin chloramphenicol streptomycin penicillin	C S F	2	47	R	R	R	S
March	slight improvement	penicillin streptomycin chloramphenicol trypsin, i. v.	Blood	6	47	R	R	R	S
			Nose, throat	15	47	R	R	R	S
April	much improved	erythromycin	Nose, throat	6	47	R	R	R	S
			Blood	1	47	R	R	R	R
May	infection controlled, mental deterioration	erythromycin chlortetracycline	Nose, throat	2	47, 47c	R	R	R	R
			Nose	1	47	R	R	R	R
			Throat	1	47, VA4	R	R	R	S
			Nose, throat,	2	6, 47, VA4	R	R	R	R
			rectum	1	6, 47, VA4	R	R	R	S
June	unchanged	chlortetracycline	Nose, throat, rectum	3	6, 47, VA4	R	R	R	S
			Nose	1	47	R	R	R	R
			Nose, rectum	2	47	R	R	R	S
July	unchanged	None	Nose	1	47	R	R	R	R
			Throat, rectum	3	47	R	R	R	S

* R—resistant

**S—sensitive

a majority of the fatal cases would have drug resistant staphylococcal infections, whether or not that influenced the outcome of therapy.

This small series of cases is representative of our clinical experience and the results are in general accord with Wise and Spink's experience. It appears that present day treatment with erythromycin and other agents results in the salvage of some cases while a considerable proportion go on to death despite any treatment.

One of the eight cases in the series is so clearly representative of the effect of the environmental factors described earlier in this report and whose source and treatment are typical of present day problems in the therapy of staphylococcal infection, that a summary of it is presented below (Table IV).

The patient was a forty-one year old taxi driver who was admitted to the neurological service following a head injury in January, 1953. After two weeks of observation a craniotomy was performed for diagnostic purposes but no specific lesions were identified. A few days later he became febrile and a culture of blood revealed Staphylococcus aureus. A day or so later the cerebrospinal fluid was also found to contain a similar organism and associated with it were the manifestations of meningitis. For two months he was treated with high doses of antibiotic regimens with included chlortetracycline, chloramphenicol, streptomycin and penicillin. In addition a short course of intravenous trypsin was administered. Despite treatment he continued to be critically ill, although several negative blood cultures were obtained in the latter part of this period. In April he was started on erythromycin which was continued for about one month. During this treatment clinical improvement was apparent with return to normal of temperature although a severe degree of mental deterioration continued to be present. He was convalescent thereafter except for a bout of diarrhea following chlortetracycline treatment of a urinary tract infection.

During the period of acute illness thirteen blood cultures, and two cerebrospinal fluid cultures were found to contain drug resistant staphylococci of group III, 47 phage type. In addition twenty-nine cultures from the nose, throat or rectum also yielded staphylococci with these characteristics.

Of particular interest was the observation that after three weeks of treatment with erythromycin a staphylococcus of group III, 47 phage type resistant to this drug was isolated from his blood, incidentally at a time when the patient gave no evidence of infection. Staphylococci of at least two other closely related group III phage types appeared during and after erythromycin treatment which alternately exhibited resistance to this agent. Ultimately, the only strains isolated were phage group 47 which were again sensitive to erythromycin.

This case illustrates several important points. First, the infection developed in the hospital and the causative strain was drug resistant and of a group III phage type which was widely disseminated among the hospital population. This finding is characteristic of infections with staphylococci which develop in hospitals and contrasts to infections which develop outside hospitals, where the organisms are more frequent-

ly drug susceptible. Second, the causative organism was found not only in the blood and cerebrospinal fluid but in the nose, throat and rectum in many cultures over a long period of time. In most cases of staphylococcal infection we have been able to isolate staphylococci of identical characteristics from lesions and mucous membranes of the patients. Finally, cure was effected with the most recently introduced antimicrobial drug to which staphylococci resistant to most other agents are usually highly susceptible.

Discussion

One cannot view the present prospects for the treatment of staphylococcal infection with optimism. The data which have been presented have revealed that mortality rates of acute staphylococcal bacteremia in the period before antibiotics ranged from 66 to 80 per cent. Following the introduction of penicillin the mortality was significantly reduced —with figures of 28 and 54 per cent in two reported series. In the recent era when erythromycin and other drugs have been generally used about one-half of the patients have died despite intensive antimicrobial therapy.

Based on this evidence we believe, therefore, that the mortality rate from acute staphylococcal bacteremia now is of the same general magnitude as it was in the early period of penicillin therapy, and that drug resistance has not been an important cause of therapeutic failures in the treatment of staphylococcal infection. This situation at first appears paradoxical since repeated observations have been made of limited effectiveness of antibiotics in treatment of infections caused by microorganisms which are resistant to them. The reasons which, to us, appear to explain this state of affairs are as follows: First, although many staphylococcal infections are caused by "drug-resistant" strains today, there has usually been available for treatment agents such as erythromycin, or earlier, the tetracycline derivatives, which were highly active against the strains which were resistant to penicillin or streptomycin. Moreover, therapeutic results with these newer agents when employed against drug susceptible infections have often been successful.

Second, since a large proportion of staphylococcal infections are caused by drug resistant strains, fatality has usually been attributed to this factor, when in actuality it has many times resulted from the natural severity of the disease and its accompanying complications such

as was also observed in the early days of penicillin treatment. It seems to us that there is an irreducible minimum of one-third to one-half of fatalities in staphylococcal bacteremia which no agent or agents now available can be expected to treat successfully.

The studies of staphylococcal carriers have revealed many details of the important relations between the occurrence of drug resistant staphylococci and antimicrobial therapy. The most striking feature of the relationship appears to be that, within certain limits, the frequency of occurrence of resistant strains is proportionate to the intensity of exposure of staphylococcal flora to the agents under study.

Such a concept will explain the occurrence of the greatest degree of drug resistance in hospitals which are centers of the most intense use of antibiotics, and their low percentage in the general population where antibiotics are used less. Furthermore, Lepper and his associates' studies with erythromycin[19] indicate that altering the amount of a drug in the hospital environment is promptly followed by a corresponding change in the degree of resistance of the staphylococcal flora to the agent.

Although the present study has tended to minimize the importance of drug resistance, as it is presently encountered, as an important explanation for fatalities in staphylococcal infections, there is no question that it should be avoided. It can be inferred from several reports that infections with drug resistant staphylococci occur in proportion to the incidence rate of drug resistant staphylococci in the environment from which they arise, and that patients introduced into a new environment will acquire, in superficial areas at least, the strains present in that environment.

All of these characteristics provide a basis for developing a degree of control of the distribution of drug resistant staphylococci in hospitals. Such a plan would be dependent upon limiting the use of one or more agents for a period of time until the staphylococci present in the environment had regained susceptibility to them. At present there is a fairly general, and almost involuntary attempt not to use erythromycin in order to save its effect for staphylococcal infections. The general problem of limiting the frequency of occurrence of drug resistant staphylococci provides a very valid incentive for the introduction of new antibiotics whose antimicrobial functions duplicate the action of presently available agents, but do not participate in cross resistance with

them. With such agents therapeutic programs could be arranged to keep in reserve antimicrobial drugs which could be expected to be active against drug resistant infections with staphylococci at all times.

The finding that a relatively discrete biological subdivision of staphylococci is the chief source of resistant strains (phage group III) raises many interesting problems for investigation. For example, it has been presumed that these strains have been selected out of a more heterogeneous population of staphylococci by exposure to antibiotics, although the reason why group III strains predominate is unknown. The question of virulence of these drug resistant strains is also unanswered and Sherris and Florey[20] have reported that wounds infected with penicillin-resistant strains show less inflammatory reaction than those caused by penicillin-susceptible strains. These and many other challenging problems await further study.

Summary

Following the introduction of penicillin, streptomycin, chlortetracycline, and oxytetracycline, there has been a progressive increase in the proportion of staphylococci which are resistant to these agents. This change has been most prominent in hospitals where the drugs are used extensively, and resistance of two-thirds to three-fourths of strains isolated has been reported from studies in several insitutions.

Newly hospitalized patients acquire resistant strains in the hospital with regularity, and staphylococcal infections which develop in the hospital are more apt to be caused by resistant organisms. Studies at Bellevue Hospital by one of the authors revealed that drug resistant hospital strains were acquired most rapidly by new patients if they received the tetracyclines in treatment, less rapidly if they received penicillin, and least in patients who received no antibiotics.

Staphylococci from non-hospitalized persons show a much lower degree of resistance which correlates with the lesser use of antibiotics in the general population.

Phage typing studies have revealed that a great majority of all drug resistant staphylococci are lysed by phages of one serologic group (III). The mechanism of this occurrence is as yet unexplained.

Reports were cited indicating that the mortality rate from staphylococcal infection at present is of the same general magnitude that it was in the early penicillin period, but lower than it was before penicillin

was used.

Analysis of the treatment of present day staphylococcal infection led to the opinion of the authors that the high mortality rate is less a result of infections caused by drug resistant strains than it is a reflection of the basic severity of the disease, and its frequent occurrence in patients with many secondary illnesses.

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PRESENT DAY PROBLEMS IN RABIES*

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THE dog is still the main vector of rabies in the western hemisphere, but certain other species have assumed importance in the spread of the disease. For example, in the rural areas of New York State in 1943, fox and cattle rabies began to appear in significant numbers until in 1946 there were reported 440 cases of rabies in cattle and 308 in foxes. The increased incidence of rabies among these species is of particular interest since it occurred concomitantly with a striking drop in the incidence of the disease in dogs. This is shown by the statistics of 1947 in which there were reported 375 cases of cattle and fox rabies as compared with only 40 dog cases. It is believed by Korns[1] that vaccination of dogs which was then being carried on helped to control the disease among these animals. We shall return to this subject later.

Another interesting aspect of the epidemiology of rabies involves the bat. Rabies was first demonstrated in vampire bats in southern Brazil in 1921 and the deduction was made that these animals were responsible for epizootics of paralytic rabies among cattle in that area from 1908 to 1918.[2] Vampire bats caused rabies among thousands of cattle in Trinidad between 1925 and 1929, and between 1929 and 1930, seventeen human beings died of rabies transmitted by the bite of vampire bats. Pawan[3, 4] showed that bats were capable of transmitting rabies by bite as long as eighty days before they showed symptoms of disease. In rare instances bats experimentally infected developed rabies but recovered completely. de Verteuil[5] showed that four vampire bats inoculated with a bovine strain of rabies transmitted the disease to twenty-five cattle although they themselves showed no symptoms of rabies. A cattle disease known as derriengue, which has been present on the west coast of Mexico for the past forty years, has been found to be due to rabies transmitted by vampire bats.[6] Rabies has appeared among insectivorous bats in Florida

* Presented at the 27th Graduate Fortnight of The New York Academy of Medicine, October 27, 1954.

and Pennsylvania.[7, 8] In Florida a lactating bat which had bitten a child was proved to be rabid. An organized hunt netted 387 bats. Rabies virus was demonstrated in the brains of six of these animals although they exhibited no symptoms.

The relative scarcity of wild animal vectors around cities makes the control of rabies easier in urban than in rural areas. This is illustrated by the experience of New York City in recent years. Rabies has not been demonstrated in any animal brain in New York City since 1949.

Certain improvements in the diagnosis of rabies in animals and human beings should be mentioned. Negri bodies are more likely to be found in the brains of animals infected with some strains of street rabies virus than with other strains. This means that the likelihood of finding Negri bodies depends upon the type of the infecting strain, as well as other factors.[9] Mouse inoculation of suspected brain material should be carried out in every instance. Surveys of large numbers of routine specimens submitted for diagnosis have shown that 10 to 15 per cent of those cases proved positive by mouse inoculation had been missed by direct microscopic examination for Negri bodies. It is also recommended that whenever possible, suspensions of the submaxillary glands of the suspected animal be injected into mice. Isolation of virus from the salivary glands furnishes definite evidence that the bite has carried with it a risk of rabies to the exposed person.[10]

Regarding the diagnosis of the disease in man, it is noteworthy that a certain percentage of patients do not show the classical clinical picture of rabies. Occasionally rabies may be mistaken for fulminating poliomyelitis. Erickson[11] has recently reported three cases which were proven to be rabies at autopsy although this disease was entirely unsuspected on clinical grounds. The diagnosis of rabies may be made by intramuscular injection of the patient's saliva into hamsters, which are extremely susceptible to the virus.

During the past ten years important advances have been made in the protection of man and animals against rabies. Before entering upon the discussion of this topic, however, it would seem worth while to try to assay the risk of contracting the disease when no attempt to avoid its occurrence is made.

Man is relatively susceptible to rabies and under some conditions the attack rate following bites is very high. For example, Koch[12] reported an instance in which nine of twelve persons bitten by a rabid

wolf developed rabies. Bites upon the face are by far the most dangerous; those on the arm and hand entail the next greatest risk of rabies, while those on the legs are less likely to be followed by the disease. The incubation period is shortest following bites upon the face. Sellers[13] states that the risk is seventy-two times as great following a face bite by a rabid dog as that following a bite on the leg. Kraus[14] reported that rabies occurred in 11 per cent of children bitten on the face despite vaccination. Bites through clothing are less likely to be followed by rabies than wounds which are directly inflicted. Contamination of mucous membranes is much less dangerous than are bites and there is little danger from virus coming into contact with unbroken skin. An indication of the over-all attack rate in the untreated individual may be obtained from the data of Schuder[15] who reported 1,325 deaths from rabies in 14,959 persons bitten by rabid animals (9 per cent) before vaccination therapy was available.

The laboratory evidence regarding the effectiveness of vaccination following exposure is not entirely convincing. There are a number of reasons for this, which we shall not discuss here. However, statistical data show quite certainly that vaccination does materially lessen the risk of rabies. Sellers[13] states that the incidence of the disease is 5 to 15 per cent following the bite of a rabid animal if no vaccination is employed, and only 1 per cent among vaccinated persons. McKendrick[16a] reports a reduced fatality rate of 0.34 per cent among nearly 153,000 vaccinated persons. It should be noted, however, that McKendrick's figures exclude cases in which there was an incubation period of less than two weeks. We shall return to this highly significant fact later in this discussion.

We can present here only a very brief synopsis of the important experimental work which has gone into the search for a satisfactory anti-rabies vaccine. Much of this work has contributed greatly to the general development of virology. Pasteur was the first to modify the characteristics of a virus by repeated passage in a species other than the natural host of the virus.[17] By serial intracerebral passage in rabbits street rabies virus was converted into fixed rabies virus. The incubation period became altered from a long, irregular interval to a short, constant or fixed one (hence the name fixed virus). Fixed rabies virus lost the ability to produce Negri bodies and by the one hundredth rabbit passage it was practically non-pathogenic for dogs when injected subcutaneously.

TABLE I—PARALYTIC ACCIDENTS FOLLOWING ANTIRABIES TREATMENT OF MAN (McKendrick)*

Vaccine	*No. Treated*	*Proportion of accidents: 1 in*
Attenuated virus (cords)	152,899	3,398
Diluted virus	75,141	3,194
Phenol-killed virus	488,795	8,887
Heat-killed virus	140,959	17,620
Ether-killed virus	90,919	10,102

* Modified from McKendrick, A. G.;[19a] *Bull. Hlth. Org. League of Nations*, 9:31, 1940.

Fixed virus is unable to multiply in non-nervous tissue, such as salivary glands. It is probable that Pasteur's virus was not made up entirely of homogeneous particles since strains derived from it show considerable variation in their immunizing capacity. Pasteur exposed fixed virus to drying at room temperature; he found that infectivity of the virus as tested by intracerebral injection of rabbits varied inversely with the length of the drying period. He showed that a graded series of subcutaneous injections of dried fixed virus protected dogs against infection with street virus.

Fermi[18] developed the first chemically treated vaccine. It was prepared by adding phenol to fixed virus suspensions; it contained active virus. Semple[19] modified Fermi's method and produced a phenolized vaccine which retained immunizing capacity although it was completely non-infectious. Vaccines have been prepared by inactivating the fixed rabies virus with chloroform, formaldehyde and ether. In 1940 we[20] employed ultraviolet light to prepare a vaccine which was antigenically potent although it contained no active virus. An excess of the inactivating chemical or of ultraviolet light makes the virus non-antigenic as well as non-infectious. The concentration of chemical or the dose of ultraviolet radiation must therefore be carefully controlled.

For many years vaccines were placed on the market with no control regarding their potency. It is possible that some of the conflicting data regarding the value of vaccines are due to this fact. Since 1940 the immunizing capacity of rabies vaccines has been tested in mice before distribution.

TABLE II—RESULTS OF INOCULATION OF DOGS INTO THE MASSETER MUSCLES WITH THE FLURY STRAIN OF RABIES VIRUS

Inoculum				*Mortality*	*Obs. Per.*
Egg Pass.	LD_{50} Titer	Dil	Vol (ml)		*Months*
22	$10^{-4.65}$	1-5	0.5 x 2	0/5*	14
22	$10^{-4.89}$	1-5	0.1 x 2	0/5*	14
74	$10^{-4.75}$	1-2. 5	0.2 x 2	0/4	6

* One dog from each of these groups was sacrificed one and two months after inoculation, respectively. Modified from Koprowski, H. and Black, J.,[25] J. Immunol., *64*:188, 1950. Reprinted by permission of the publishers, Williams & Wilkins Company.

All vaccines described thus far are made from infected rabbit brain tissue. Thus, they may be followed by neuroparalytic accidents. Such accidents occur more commonly with vaccines containing active virus—about once in 3,300 times as compared with once in 8,800 to 17,000 times with vaccines which have been completely inactivated. Table I shows McKendrick's data on incidence of neurologic complications following approximately 150,000 treatments with anti-rabic vaccine.[16a]

It is worth noting that in smaller groups of persons the incidence of neurologic complications has been much higher. For example, in Los Angeles County there were such complications once per 1,194 treatments.[16b] The incidence of post-vaccination complications is highest in persons treated previously, and in those who are allergic.

Since the dog is so greatly involved in the spread of rabies many attempts have been made to produce a vaccine for immunization of these animals before they are exposed to the disease. Some of these attempts have achieved a large measure of success. Umeno and Doi[21] used a phenolized vaccine which contained some active virus. In Japan they vaccinated dogs on a large scale with a single large dose of vaccine. Their efforts were successful. Johnson[22] states that 2,000,000 dogs were vaccinated in the United States between 1922 and 1928 with a single injection of a vaccine of the Umeno type. No reliable statistics of the results were obtained. One case of rabies due to the vaccine occurred among 30,000 vaccinated dogs in Japan and paralytic rabies due to the vaccine was observed among vaccinated dogs in rare instances in the United States. This caused the U. S. Department of Agriculture to enforce the use of vaccine containing no active virus. This course was

TABLE III—RESULTS OF CHALLENGE WITH STREET VIRUS OF DOGS VACCINATED WITH EGG-ADAPTED FLURY STRAIN RABIES VIRUS

Vaccine	*Interval between vacc. & challenge*	*Results of Challenge Inoculation with Street Virus*		
Egg Passage		LD_{50} titer in Mice	*Mortality ratio of dogs*	
			Vaccinated	*Controls*
	weeks			
86	5	$10^{-6.75}$	0/6	3/6
40	9	$10^{-6.25}$	0/9	8/15
40	7	$10^{-6.25}$	0/7	10/10
60	3	$10^{-5.00}$	0/8	8/9
		Or		
74*	5	$10^{-6.75}$	0/6	
74	27	$10^{-6.25}$	0/4	
75	5	$10^{-6.00}$	0/4	3/6
77	7	$10^{-6.25}$	0/10	
79	3	$10^{-5.00}$	0/8	
80	5	$10^{-6.00}$	0/6	
84	7	$10^{-6.25}$	2/8	

* 5ml of 40 per cent chick embryo suspension used as inoculum—in all other instances each animal received 5ml of a 20 per cent chick embryo suspension.

Modified from Koprowski, H. and Black, J.,[25] J. Immunol. *64*:190, 1950. Reprinted by permission of the publishers, Williams & Wilkins Company.

unjustified since fixed rabies virus does not multiply in the salivary glands and is not found in saliva. The Semple type of vaccine produced to meet safety requirements proved ineffective. An improved canine Semple type of vaccine was marketed after introduction of the mouse-potency test. This vaccine produced good immunity in dogs. A single injection afforded protection for a year.[1, 22]

A much more effective and longer lasting immunity can now be obtained with a living attenuated virus vaccine—the Flury chick embryo adapted rabies virus.[23] The Flury strain was isolated by Johnson[24] from the brain of a child infected through the vagina. It was obtained by direct intracerebral inoculation of one-day old chicks. It was then passaged serially in chicks. It is the only strain of rabies virus which has been maintained entirely in non-mammalian hosts. Thus, there was produced a rabies virus strain fixed in chick brain. The fixed chick brain virus showed a greatly lessened pathogenicity for rabbits, mice and dogs.

When the living fixed chick brain virus was inoculated into dogs, paralytic rabies was produced but virus was not found in the salivary glands or saliva. The 136th chick brain passage was then successfully cultured in the yolk sac of the developing chick embryo by Koprowski and Cox.[23] After the 16th passage in the chick embryo, the titer of the virus became constant. It was found to be non-pathogenic for rabbits when inoculated intramuscularly. Experiments with the 22nd and later passages of the Flury strain showed that the virus was entirely innocuous when injected into the masseter or thigh muscles of dogs. The saliva and brains of these animals contained no virus (see Table II).

Despite its lack of pathogenicity when given intramuscularly, the virus remained capable of producing rabies in these animals when injected intracerebrally.[25] Seventy-six dogs were vaccinated by intramuscular injection of live egg adapted Flury virus. Each dog received 2 to 5 cc. of a 20 per cent suspension of chick embryo. The animals proved to be resistant when challenged by street rabies virus given by intramuscular injection, five to twenty-seven weeks after vaccination.[25] Only two of the seventy-six vaccinated animals died as compared with thirty-two deaths among forty-six un-vaccinated animals (see Table III).

Koprowski and Cox[23] inoculated 199 dogs by intramuscular injection in their laboratory without production of rabies in any case. Later they injected 6,757 dogs on Staten Island with 5 cc. of the embryo suspension. Subsequent work has shown that the Flury rabies vaccine confers a solid degree of protection for two or three years to vaccinated dogs against massive challenge doses of street virus.[26] The Flury vaccine appears to be superior to phenolized vaccines and other attenuated vaccines as regards both the degree and duration of the immunity. Statistical analysis indicates the superiority of the protection afforded one and two and three years after vaccination with the Flury strain as compared with phenolized virus vaccines.[27] This result may be considered in keeping with the general superiority of the immunity produced by living virus vaccine as compared with chemically attenuated or killed virus preparations. More than one million dogs have been vaccinated with the Flury vaccine and in no instance has the modified virus shown a tendency to regain its original virulence and its ability to be transmitted (see Table IV).

The value of the Flury egg adapted living rabies virus was shown very clearly in Malaya during 1952 and 1953.[28] The high enzootic level

TABLE IV—RESULTS OF 39 MONTHS' IMMUNITY TEST IN DOGS VACCINATED WITH DIFFERENT TYPES OF RABIES VACCINE*

Authors	*Type of Vaccine*	*Mortality Ratio*
U.S. Public Health Service in cooperation with Lederle	Phenolized (commercial)	8/34 (23.5%)
	Ultra-violet (commercial)	7/30 (23.3%)
	Avianized (Flury) Lederle	0/30 (0%)
	Controls (non-vaccinated)	31/36 (86.1%)

* From Cox, H. R.,[28] Brit. med. J., July 31, 1954. Reprinted by permission of the British Medical Journal.

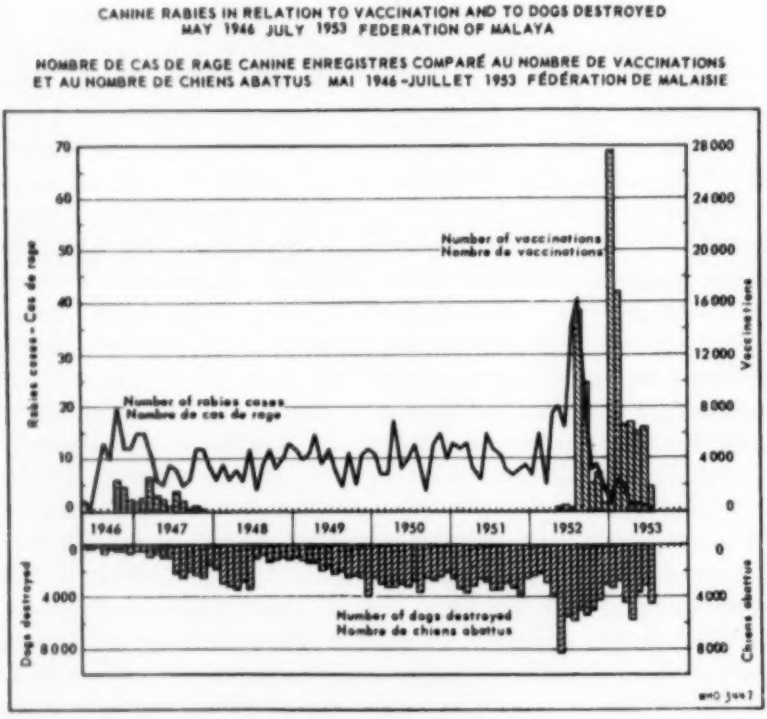

CHART I

From the World Health Organization Technical Report Series No. 82;[29] Expert Committee on Rabies, Second Report, April 1954, page 24. Reprinted by permission of the World Health Organization.

of rabies in Malaya reached epizootic proportions in the middle of 1952 (See Chart 1). At this time 18,000 dogs were vaccinated with chick embryo Flury vaccine and 12,000 dogs were vaccinated with phenolized nerve tissue vaccine. During January 1953 through July 1953 a mass canine immunization campaign using Flury vaccine alone was carried out all through Malaya. During this period 73,000 dogs were vaccinated. Chart 1 shows a sharp fall in dog rabies which occurred between August 1952 and August 1953, and the relation of the dog vaccination to this fall. During August 1952 when the mass immunization program was begun, there were forty-one laboratory confirmed cases of dog rabies. By June 1953 there were no cases of rabies, and no cases of rabies in man or animals have been reported from Malaya between June 1953 and December 1953.

It seems clear that vaccination of dogs with an effective vaccine such as the Flury vaccine is an important measure in control of rabies. It is particularly useful when rabies exists in the wild animal population, but vaccination must be combined with other control regulations such as licensing of all owned dogs and the collection and destruction of stray dogs.

Recent changes which have occurred in the Flury egg virus have indicated that it may eventually prove to be safe for human immunization. This change has to do with the loss of pathogenicity of the virus when injected into the brains of adult mice, rabbits and dogs.[29] The loss of pathogenicity occurred spontaneously around the 180th egg passage of the virus. It has not been accompanied by a loss of the immunizing power of the virus. Of theoretical interest is the observation that the high passaged Flury virus is not homogeneous but made up of two types of virus particles.[30]

It has already been demonstrated[31] (Lederle Laboratories, personal communication), that human volunteers given as little as 0.1 gram of Flury vaccine intradermally have developed demonstrable neutralizing antibodies about thirty days after the injection. When given a booster dose ten to twelve months after the initial injection, their sera in high dilution have protected mice against 30 MLD of street virus given intracerebrally. The advantages of Flury vaccine over chemically killed or attenuated vaccine containing nerve tissue are obvious. However, it is not yet ready for general use for human beings.

We have stated that anti-rabic vaccine given after exposure fre-

TABLE V—SERUM VS. VACCINE PROPHYLAXIS OF RABIES IN GUINEA PIGS TREATMENT ADMINISTERED AT VARYING INTERVALS AFTER VIRUS INOCULATION

Treatment	*Time from virus inoculation[3] to treatment (hours)*	*Number guinea pigs*	*Rabies Deaths*
2 cc. serum[1]	3	10	1
2 cc. serum	24	10	3
2 cc. serum	48	10	6
Vaccine[2]	3	10	4
Vaccine	24	10	3
Vaccine	48	10	5
Controls	—	5	5

[1]=1 dose unconcentrated rabbit immune serum subcutaneously.
[2]=2 cc. 5 per cent phenolized vaccine subcutaneously daily for 10 doses. Vaccine potency 1,000 MLD.
[3]=0.25 cc. of 1/5 supernatant dog brain street virus in masseter.

From Habel, K.,[31] Pub. Health Reports, 60:551, 1945. Reprinted by permission of the Department of Health, Education, and Welfare, Public Health Service, Washington, D.C.

quently fails when the incubation period is short. The reason for this failure is assumed to be due to the fact that the virus reaches the central nervous system and spreads up it to the vital neurones before immunity can be produced by the vaccination process. It has been shown that virus inoculated into the muscle remains viable at the site of inoculation, and may invade the spinal cord within three or four days. Vaccination could not be expected to produce immunity before the virus reaches the central nervous system. Hyperimmune rabies serum might be of value in neutralizing virus at the site of inoculation, and might retard the spread of virus up the cord until vaccination could bring about the development of the neutralizing substances which have been demonstrated in the cord of vaccinated animals.

Many attempts[32, 33] have been made to produce a useful hyperimmune serum since Babès and Lepp[34] first showed rabicidal antibodies in serum of immunized animals. Most of these experiments were inconclusive, for a number of reasons. However, Habel[31] in 1945 produced a rabbit hyperimmune serum which seemed to afford a definite degree of protection when given to guinea pigs within 48 hours following intramuscular injection of street virus (see Table V).

Koprowski and Van der Scheer[35] prepared a concentrate of serum obtained by injection of rabbits, sheep and horses with Flury egg virus.

TABLE VI—COMPARATIVE PROTECTION OF HAMSTERS TREATED WITH ANTISERUM OR VACCINE

Type of Protective Treatment	*Dilutions*	*Mortality Ratio of Hamsters Infected with Virus Dilutions*	
		*1:160**	*1:320***
Antiserum	1:2	1/10	
	1:4	2/10	
	1:8	2/10	
	1:16	4/10	1/10
	1:32	6/10	3/10
	1:64	10/10	5/10
Semple vaccine	1:20	10/10	10/10
	1:5000	10/10	10/10
Untreated controls		10/10	10/10

* Contained 40 LD_{50} of virus.
**Contained 20 LD_{50} of virus.

From Koprowski, H., Van der Scheer, J. and Black, J.,[88] Amer. J. Med., *8*:414, 1950. Reprinted by permission of the authors and the Journal.

TABLE VII—NEUTRALIZATION TESTS OF SERA FROM INDIVIDUALS TREATED WITH EITHER ANTISERUM AND/OR VACCINE

	Protective Titer of Serum Obtained					
			*Days after First Injection of Vaccine***			
Case	*Before Treatment*	*One Day after Serum Injection**	*3*	*7*	*14*	*30*
T.J.	<1:2	1:50	1:65	1:70		1:55
75	<1:2			<1:2	1:4	
86	<1:2			1:4		
15					<1:2	1:3
124				<1:2	<1:2	
43				<1:2	1:16	

* Antirabies serum concentrate administered within three hours after exposure.
**Seven-day course of phenolized vaccine initiated twenty-four hours after exposure.

From Koprowski, H., Van der Scheer, J. and Black, J.,[88] Amer. J. Med., *8*:418, 1950. Reprinted by permission of the authors and the Journal.

TABLE VIII—INDICATIONS FOR SPECIFIC POST-EXPOSURE TREATMENT

Nature of Exposure	Condition of biting animal: At time of Exposure	Condition of biting animal: During Obs. Period of 10 days	Recommended Treatment
I. No lesions; indirect contact only	rabid	——	none*
II. Licks:			
(1) unabraded skin	rabid	——	none*
(2) abraded skin & abraded or unabraded mucosa	(a) healthy	healthy	none
	(b) healthy	clinical signs of rabies or proven rabid	Start vaccine first signs of rabies in animal
	(c) signs suggestive of rabies	healthy	Start vaccine immediately; stop treatment if animal normal on 5th day after exposure**
	(d) rabid, escaped, killed or unknown	——	Start vaccine immediately
III. Bites:			
(1) simple exposure	(a) healthy	healthy	none
	(b) healthy	clinical signs of rabies or proven rabid	Start vaccine at first signs of rabies in animal
	(c) signs suggestive of rabies	healthy	Start vaccine immediately; stop treatment if animal normal on 5th day after exposure**
	(d) rabid, escaped, killed, or unknown; or any bite by wolf, jackal, fox, or other wild animal	——	Start vaccine immediately
(2) severe exposure: (multiple; or face, head, or neck bites)	(a) healthy	healthy	hyperimmune serum immediately; no vaccine as long as animal remains normal
	(b) healthy	clinical signs of rabies or proven rabid	hyperimmune serum immediately; start vaccine at first sign of rabies
	(c) signs suggestive of rabies	healthy	hyperimmune serum immediately, followed by vaccine; vaccine may be stopped if animal is normal on 5th day after exposure
	(d) rabid, escaped, killed or unknown. Any bite by wild animal	——	hyperimmune serum immediately, followed by vaccine

* Start vaccine immediately in young children and in patients where a reliable history cannot be obtained.

**An alternative treatment would be to give hyperimmune serum and not start vaccine as long as the animal remained normal.

NOTE: To be effective hyperimmune serum must be given within 72 hours of exposure. Dose: 0.5 ml per kg of body-weight.

Serum given twenty-four hours after intramuscular injection of street virus protected hamsters while a course of injections of phenolized rabbit brain failed entirely. Serum was less effective when given seventy-two hours after injection of virus. Beyond this interval it had no effect (see Table VI).

Further experiments[36] showed that administration of serum does not interfere with immunizing capacity of Flury egg vaccine.

Serum was given to a patient soon after exposure together with a course of Semple vaccine. The serum of this patient showed a high titer of protective antibody during the next thirty days. In contrast, five patients who received only Semple vaccine showed only a very low antibody titer during this time (see Table VII).

Hyperimmune serum has been used to treat human beings after exposure to rabies. Some reports suggest that serum is effective, particularly in face bites.[37] The number of persons treated is too small to permit a significant statistical analysis. However, the experimental evidence favoring serum is so great that it is recommended that serum followed by vaccine be used in all human cases of severe exposure. Serum should be given as soon as possible after exposure since it appears to be ineffective unless it is administered within seventy-two hours. Table VIII shows serum may be given in instances other than those involving severe exposure.[10]

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GROUP PSYCHOTHERAPY IN PATIENTS WITH PEPTIC ULCER*

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It is well known that a certain number of patients with peptic ulcer do not respond to the usual medical and surgical treatment. In these patients the presence of persistent emotional tensions has long been recognized as one of the etiologic factors and some of these have responded favorably to psychotherapy. Group psychotherapy is one of the newer psychotherapeutic techniques that offers promise in the treatment of patients with chronic peptic ulcer. Two reports, one by Chappell[1] (1937) and the other by Selesnick[2] (1950) indicated good results when group psychotherapy was used in treating patients with peptic ulcer. Also, since current views postulate similar underlying emotional factors in patients with peptic ulcer, namely, a conflict between unconscious oral-aggressive and dependent needs and the conscious ego demands to be self sufficient, it was thought that a psychotherapeutic group might help the patients to understand and work through these common conflicts.

The treatment of this group of ulcer patients was begun in October 1948 and continued until May of 1950. A total of fifteen patients participated in the group at one time or another. The ages ranged between twenty-eight and fifty-eight years and there were five men and ten women in the group.

The selection of patients for the group was on the basis of their physical condition. Originally it had been planned to include only patients with uncomplicated chronic duodenal ulcer who had received medical treatment alone. Practically, this proved to be impossible because there weren't enough such patients who had time available for group psychotherapy. While all of the patients had originally had duodenal ulcers with characteristic symptoms and x-ray findings, only

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eleven of these who finally entered the group had uncomplicated chronic duodenal ulcer. Of the remaining four, one had had a hemorrhage, one had had a vagotomy, and one had had a vagotomy and later a subtotal gastrectomy, and the fourth had had a hemorrhage and then a subtotal gastrectomy.

The duration of the condition ranged from two to fifteen years with most patients having history of persistent gastrointestinal symptoms from two to four years prior to beginning group treatment. From the standpoint of persistence of symptoms and failure of response to the usual type of medical and surgical treatment, all of these patients belonged to that group of ulcer patients that were considered by the gastroenterologists to be refractory or intractable ulcer cases.

With one exception, a forty-nine year old woman who had arthritis, none of the patients had any other physical disease. However, they all had one or more other physical complaints—such as headaches, dizziness, back pains, etc.

The underlying psychiatric condition had not been considered at all in selecting the patients for the group, but, as was anticipated, this turned out to be the most important factor of all. Psychiatric examination and psychological testing revealed the following: Five of the patients (three men and two women) were found to have I.Qs. in the dull normal range, the rest had average intelligence ratings. All of the patients showed chronic neurotic symptomatology; in some this was quite marked, in others it was less severe. The most frequent neurotic symptoms were a reactive type of depression with anxiety; many showed hysterical and/or compulsive traits, and in two of the men, a definite hypochondriacal preoccupation was present.

More important than the neurotic symptomatology were the severe underlying personality disturbances that all of those patients showed. All of them were found to have rigid, immature, severely constricted personalities and to function at a restricted level mentally, which may explain the low I.Qs. One man and two women were definitely schizoid. Another man was probably a borderline psychotic with a questionable history of transient auditory hallucinations. Two of the women had poorly defined paranoid tendencies. Of the remaining three men, two were ineffectual, passive, dependent individuals both of whom had marked sexual difficulties; the third man was an extremely tense, compulsive character. The remaining women in the group all had

severe characterological disturbances, including three who were overtly aggressive women with rigid compulsive characters, and two who showed severe masochistic characters.

One other point should be stressed in relation to those patients. In fourteen of the fifteen patients, there was evidence in the psychiatric history that the time of the onset of the ulcer symptoms coincided with the loss or threat of loss of a parent or a parent surrogate, most often the mother. In six of the patients, the coincidence was quite definite, as follows: In one patient, ulcer symptoms occurred right after the onset of severe hypertension in the mother; in a second, ulcer symptoms began after the death of the father which was followed by a heart attack in the mother; in the third and fourth patients, the death of an older sister who was like a mother was immediately followed by ulcer symtoms; in a fifth patient, symptoms began at the time the mother was operated on for cancer of the rectum; and in a sixth patient, her husband was operated on for brain tumor and left aphasic and paralyzed, following which she developed an ulcer. In the remaining eight patients, while the time coincidence was less definite, their ulcer symptoms were related to similar types of events such as separation or threat of separation from a loved object.

The group psychotherapy used with these patients was a psychoanalytically oriented group psychotherapy in which the spontaneous productions of the patients comprised the material of the sessions. The group therapist participated only to help bring out the emotional factors underyling the patients' productions and to make appropriate interpretations concerning these.

The patients were prepared for the group psychotherapy by one or two individual interviews with the group therapist. These interviews served to acquaint the patient with the group therapist and were, through him, the patient's initial link with the group. As a result, the patient usually had a favorable attitude toward the group treatment and the group therapist even before he entered the group, because he felt he was being selected for a special kind of treatment.

The group met once a week for a period of an hour and a half in one of the rooms in the psychiatric clinic. The atmosphere was quite informal without any special seating arrangement. A brief description of the course and content of the group sessions will now be given.

The first few sessions dealt with the patients' symptoms, and during

the discussions, it became evident that there was a great sense of guilt and isolation connected with their being ill. This sense of isolation was quickly relieved by the patients realizing that others were in the same situation and felt the same way, while the tolerant attitude of the therapist helped to lessen their extreme guilt feelings.

More specific and personal material then began to be discussed and patients complained that their families didn't believe that they were sick and couldn't work. During this early phase, the group attitude towards this, even by the very patients who had complained, was that the families were right—they weren't really sick and should work. In the discussions, the group was helped to develop a more accepting attitude towards their illness.

As soon as this occurred, the patients began to express their underlying resentment, first in a very guarded way and then gradually more directly and emphatically. During this phase, the more aggressive patients took the lead and carried with them the less aggressive ones.

When the group, with the aid of the therapist, could tolerate the expression of resentment, the underlying dependent attitudes that had been foreshadowed began to emerge. Expression of these needs was encouraged by finding that others shared the same feelings and by the fact that the group accepted them. Stimulated by one patient's grief over a deceased sister upon whom she had been very dependent and guided by the therapist, the patients began to clearly express their dependent needs.

None of this was brought out in as orderly a fashion as has just been described, but only indirectly and with much wandering back and forth. Nor was it expressed as freely as might seem from the above. The underlying guilt of the group lessened gradually, and very slowly. There were constant monotonous repetitions that it was wrong to feel this way, one had responsibilities and obligations, you can't be selfish, etc.

After a long while, when the group had learned to work together well, more specific details of conflict in relation to their families were brought out. Feelings of deprivation and frustration, hurt, resentment, jealousy and rivalry were verbalized, although with a good deal of restraint which diminished only gradually and never entirely disappeared. Strong passive dependent longings, intense greedy desires for all sorts of things, and deep-seated sexual conflicts were hinted

at or expressed in terms of their derivatives. This was true also of strong sado-masochistic attitudes that most of the group had. In the later stages of the group discussion, the patients clearly indicated they saw and reacted to other patients in the group as they would to members of their families—the father, the mother and the siblings and the therapist could utilize these reactions to interpret many of these attitudes to the group.

In the beginning, the group's attitude was not only intolerant but extremely rigid. They could see themselves and their situation in relation to others only in a narrow, overly-critical fashion and it seemed to them nothing could be done to improve things. Then somewhat more flexible attitudes began to appear; situations and relationships began to be viewed in more realistic terms and the patients began to help each other to figure out ways of changing and improving these situations and relationships.

Now for a brief word about the dynamics of the group psychotherapy. This centers entirely on relationship of the patients to each other and to the therapist. The therapist, despite his informal and non-authoritative role, is the central figure to whom the patients react emotionally and he sets the "tone", so to speak, of the group by his accepting, tolerant attitude. The patients are also aided in expressing and working through their problems by establishing an identification with the therapist. The patients, through having the same symptoms and the same relationship to the therapist, also identify with each other, and from these identifications they are helped to perceive and verbalize their emotional conflicts. The group forms a unit comparable to the family, with the therapist as a sort of parental figure and the patients as siblings. It is these emotional ties in the group that offer the patient an inducement to withdraw from his neurotic isolation and provide the libidinal energy necessary to work out his problems.

Finally, certain special characteristics of group psychotherapy should be mentioned to indicate some of the mechanisms involved. The relationship to the therapist is an aim-inhibited one and therefore much less threatening to the patients. This relationship is made easier for the patients by the presence of other patients, so that the transference is "diluted" so to speak. The presence of others also provides reciprocal support and lessens the emotional pressure on the individual patient. The group supplies specific stimuli and enables patients to by-pass

resistance by the mechanisms of projection and denial, although these are less intense and on a more realistic level than in individual therapy and hence are more accessible to therapeutic influence. The group atmosphere is much more realistic so that there is a definite pull toward reality orientation and less need to retreat into fantasy. Each patient has a greater opportunity to see his own social role and the responses to his behavior in a non-threatening fluid atmosphere that encourages a more objective view and fosters relearning. The restrictions of harsh super-ego attitudes are gradually overcome by identification with the tolerant attitude of the therapist and by a process of sharing the guilt with the other patients. The development of emotional ties with the other patients diminishes the feeling of emotional deprivation and leads to better contact and the establishment on a realistic social level of satisfying object relationships.

Of the fifteen patients in the group, three dropped out after a few sessions. The remaining twelve patients all attended the group sessions fairly regularly, though some entered the group after it had been in existence for several months.

The results obtained with the use of group psychotherapy with these twelve patients can be summarized as follows: From the psychiatric point of view, three were considered unimproved, including one woman who dropped out after three months of treatment; five were considered slightly improved; two were considered moderately improved; and two were considered much improved. From the standpoint of ulcer symptoms, the results are as follows: Two patients were symptom free, three and four years respectively after the end of the treatment; four were much improved in that they had only occasional mild episodes of epigastric discomfort two years after stopping treatment; two were considered moderately improved reporting brief episodes of moderate epigastric distress about twice a year, but these were very much less frequent and less severe than prior to the group treatment; one was considered only slightly improved having three to four attacks a year but these were much less severe and more easily controlled by medication than previously. Three patients were unimproved and continued to have persistent severe attacks of ulcer symptoms. Two of these were ulcer patients and the third was a post-gastrectomy patient.

The results from the psychiatric standpoint in general coincided with the results from the standpoint of ulcer symptoms. The only

differences were as follows: One patient, the woman who dropped out after three months and who was considered unimproved from the psychiatric standpoint, did show a slight but definite improvement as far as her ulcer symptomatology was concerned. Four patients who were considered only slightly improved psychiatrically showed much improvement in their ulcer symptoms. Otherwise the degree of psychiatric improvement tended to coincide with the degree of improvement of the ulcer symptoms.

These results with the use of group psychotherapy in the treatment of ulcer patients can be roughly compared with the results reported by Stine and Ivy[8] (1952) in a survey of the effect of psychoanalysis on the course of peptic ulcer. Of the seven suitable cases they could evaluate who had been treated by psychoanalysis for periods from one to six years (140 to 628 hours of treatment) two were unimproved and five were improved, though only two of these last had no recurrence of ulcer symptoms after analysis.

In evaluating the influence of the group psychotherapy from the standpoint of ulcer symptomatology, the above results can be considered to convey only an approximate impression of its effectiveness. Originally it had been planned to set up a control group and to carefully check on diet, medication, and other factors with both groups. This proved to be impossible for many reasons, and finally, the only feasible way of checking the ulcer symptoms was to have an observer other than the group therapist follow all the patients in the group. In view of the many factors that are known to influence the course of peptic ulcer, the above results cannot be considered to be exact but they do convey the clinical impression of a careful and experienced observer.

From the psychiatric point of view the clinical impression as to effectiveness of the group psychotherapy was quite definite. All of the patients who showed any degree of improvement became less anxious and depressed, their somatic complaints (other than the ulcer symptoms) lessened or disappeared, they were less guilty and more flexible in their attitude toward their illness. All of the patients became aware to some extent of the relationship of emotional tension to their symptoms. The patients who showed more than a slight improvement became somewhat freer in their ability to express feelings, and were able to begin to work out less rigid and more adequate approaches to their life situations. Relationships to their families began to become

more realistic and more satisfying. Thus, while the group psychotherapy did not eradicate the basic personality deformities in this very sick group of patients, it did enable them to lessen their emotional tensions and it helped them to loosen to some extent their rigid patterns of reacting. This seemed to be enough to influence favorably the course of their peptic ulcer symptomatology.

The experience with this group of ulcer patients has indicated that they all showed, among other things, deep-seated conflicts between oral-dependent and oral-aggressive drives and the harsh restrictions of a rigid super-ego. This is in accordance with the findings of many other observers. No specific correlation between this type of conflict and ulcer symptoms could be drawn from our experience. Intense orality was only one of the regressive features these patients showed, although it was one of the most prominent ones.

A more important finding, common to all of these patients, was the nature of their object relationships, and in connection with this, some specific relationship to the onset of ulcer symptoms seemed apparent. As is very frequently found in patients with so-called psychosomatic disease, these patients all had intense infantile object relationships of the narcissistic type. This was especially true of their relation to their mothers, which was of the "symbiotic" type. In one session, this was strikingly brought out when four patients, three women and one man, described how tremendously affected they were by illness in their mothers and how in turn, the mothers were so concerned about the patients' illness that they watched over the patients incessantly. Similar relationships were described in connection with husbands, wives and sisters, all mother surrogate figures. Identification with and introjection of the mother figure is one of the results of this type of relationship and is associated with intensely felt and deeply repressed passive oral-dependent and oral-sadistic drives. When loss of this mother object was threatened or occurred, these patients reacted by developing ulcer symptoms. As already stated, evidence for this was found in fourteen of the fifteen patients.

Patients of this type are almost invariably difficult to treat in individual psychotherapy. Contact is not easily established, the close relationship to the therapist is too anxiety provoking, and resistance is increased by the need to ward off regressive fantasies. Group psychotherapy, from the experience with this group, seemed to enable them

to enter into the psychotherapeutic process much more readily. The reasons for this have already been noted. From the very outset, every member of this group of very ill patients participated in the group psychotherapy, and on this basis it would appear to have a definite usefulness in the treatment of severely regressed patients with chronic peptic ulcer symptoms.

Summary

1. A group of fifteen patients with chronic peptic ulcer was treated with psychoanalytic group psychotherapy for a period of eighteen months.

2. All of the patients had severe underlying psychiatric difficulties.

3. Of the twelve patients who remained in treatment, three were unimproved and the remainder showed varying degrees of improvement both in their psychiatric and ulcer symptomatology.

4. Group psychotherapy appears to have definite usefulness in aiding patients, in whom chronic peptic ulcer is associated with a regressed, rigid type of personality, to participate readily in the psychotherapeutic process.

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REPORT ON DRUG ADDICTION

BY

THE NEW YORK ACADEMY OF MEDICINE*

COMMITTEE ON PUBLIC HEALTH**

SUBCOMMITTEE ON DRUG ADDICTION***

UNDER date of January 14, 1955, there was presented to the Senate of the United States by Senator Frederick G. Payne, Republican, of Maine, a joint resolution "to provide for a more effective control of narcotic drugs, and for other purposes." Co-sponsoring the Resolution with Senator Payne were forty-two other Senators from all areas of the Nation and from all political parties, including Independent Senator Wayne Morse of Oregon.

The Interdepartmental Committee consisting of representatives from the Department of State, Department of the Treasury, Department of Defense, Department of Health, Education and Welfare, and the Department of Justice requested the Committee on Public Health of The New York Academy of Medicine to study this bill and submit a report. By the time the Subcommittee on Drug Addiction of the Committee on Public Health had an opportunity to convene it was informed that the narcotics bill had not come out of committee. However, representatives of the Interdepartmental Committee requested that the Committee on Public Health consider the narcotics problem and propose measures for suitable legislation.

Today a number of cities are raising a hue and cry of apprehension and alarm over drug addiction. Charges and claims about it appear in the headlines, coupled with demands for action of the usual kind: crackdown by the enforcement officials. Presently it is linked with the larger problem of juvenile delinquency as one of its most serious components. Before attempting to appraise the existing situation, it is helpful to look at the legal provisions and administrative bodies designed to control narcotic traffic and addiction.

LAWS AND ADMINISTRATION

International Background: At the instance of the United States Government, the conference of the International Opium Commission convened in Shanghai in 1909 in an effort to obtain international action to control the traffic in opium and its products. The Commission recommended that drastic measures be taken by each government in its own territories to control the manufacture, sale and distribution of opium derivatives. Three years later the representatives of twelve world powers met at The Hague to formulate the recommendations of the Com-

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*** Report prepared by Subcommittee on Drug Addiction, comprised of: Hubert S. Howe, M.D., Chairman; Linn J. Boyd, M.D.; McKeen Cattell, M.D.; Milton J. Goodfriend, M.D.; Arthur Voae Greeley, M.D.; Lawrence C. Kolb, M.D.; Asa L. Lincoln, M.D.; Bernard J. Pisani, M.D.; Dickinson W. Richards, M.D.; Conrad M. Riley, M.D.; H. D. Kruse, M.D., Secretary.

mission into an international convention. Here was reached the first important international agreement on the subject, which is known formally as the International Opium Convention of 1912, and popularly as the Hague Convention of 1912. This Convention was designed to bring about the gradual suppression of the abuse of opium, its products and derivatives, and cocaine. The signatory powers contracted to enact effective laws, or regulations, for the control of the production and distribution of raw opium; for prevention of export of raw opium to countries which shall have prohibited its entry; for control of the export of raw opium to countries which restrict its import; and for restricting both import and export of raw opium to that made by duly authorized persons. They further agreed to take measures for the gradual and effective suppression of the manufacture, distribution and use of prepared opium. They also engaged to exert efforts to restrict the import and export of morphine and cocaine preparations to authorized persons and to limit the manufacture, sale and use of these drugs exclusively for medical and scientific purposes.

Federal Background: Congress has no power to legislate for the mere purpose of restraining the purchase of opiates and other drugs. Rather, its power to enact Federal legislation regulating all phases of the production, manufacture, sale and use of narcotic drugs derives from the commerce clause and the tax clause of the United States Constitution. Under the commerce power, it may forbid the importation of drugs and make the violation of the statute a criminal offense. Under its taxing power it has been held that Congress may prohibit all purchase or sale of narcotics except in or from the original stamped package.

On these constitutional bases, Federal legislation effectuating the Convention to bring about legal control of narcotics with restriction on their sale and use is contained in a series of statutes. In 1909 Congress adopted a law entitled "An Act to Prohibit the Importation and Use of Opium for Other Than Medicinal Purposes." Five years later, in fulfillment of the obligations of the United States under the Hague Convention of 1912, this law was amended to prohibit the export of narcotic drugs except to a country which regulated their entry.

In that same year, in further implementation of the Hague Convention, this country enacted its basic narcotic law, the Harrison Narcotic Act. As an exercise of Federal power to tax, it was enacted as a revenue measure; but by imposing penalties for illegal manufacture and distribution, the effect of its provisions is to regulate the production, manufacture and distribution of narcotics, particularly to limit the availability of narcotic drugs to medical and scientific use. Thus, in an attempt to minimize the spread of narcotic addiction, the Harrison Narcotic Act has been applied as a measure to control the domestic narcotic traffic.

In growing recognition that there was need for a more comprehensive measure of control over import and export of narcotic drugs than was provided by the Act of 1909, as amended in 1914, an extensively revised form of this older statute was re-enacted by Congress in 1922 as the Narcotic Drugs Import and Export Act. It authorized the importation of only such quantities of opium and coca leaves as the then Federal Narcotics Control Board found to be necessary to meet medical needs. With this legitimate exception, importation of any form of narcotic drug was prohibited. Exportation of manufactured narcotic drugs and preparations was permitted under a system of control designed to assure their use for medical purposes only in the country of destination. Under the special amendment to this statute in 1924, the legal manufacture of heroin in the United States ceased.

With evidence of growing abuse of marihuana, the Congress enacted the Marihuana Tax Act of 1937, which requires the registration and payment of a tax by persons who produce, import, manufacture, sell, or transfer marihuana. When

growing of the opium poppy, ostensibly for seed yield, sprang up as the result of a shortage of imported poppy seed during World War II, the Congress enacted the Opium Poppy Control Act of 1942, which prohibited the growth of the opium poppy in the United States except under a special license issued only upon a demonstrated need for domestic production of the opium poppy to supply opium derivatives for medical and scientific uses.

Because the Harrison Narcotic Act has been used to exert control over domestic trade in narcotics, its constitutionality has been debated and subjected to test. Although nominally an application of the government's taxing power, the real function of the Act through its provision for penalties for illegal manufacture and distribution has been to restrict the distribution of narcotics to medical and scientific uses only and thereby to attempt to minimize the spread of narcotic addiction. Several cases have arisen testing the constitutionality of the Act on the grounds that it is not really a tax measure, but rather an indirect method of invading the police powers of the states; that it undertakes to regulate matters within the exclusive control of the states; and that the penalties amount to a denial of due process of law. The point at issue in test cases on the constitutionality of these statutes has been the extension of indirect control by the Federal government over objects which it is forbidden to regulate directly. The Harrison Narcotic Act has twice been declared constitutional by the Supreme Court, solely as a revenue measure and as an exercise of the Federal power to tax.

Administration: Originally the Federal Narcotics Control Board had the responsibility of control over narcotic drug imports and exports. The duty of enforcing the Harrison Narcotic Law was assumed by the Bureau of Internal Revenue through its field officers engaged in enforcing all internal revenue laws. There was no separate, specialized group of officers bound exclusively to the duty of enforcing this statute. With a growing realization of the inadequacy of such an arrangement for law enforcement to cope with the control of narcotic drug traffic, the Congress in 1930 established the Bureau of Narcotics in the Treasury Department. To this Bureau were transferred all functions and duties of control over narcotic drug imports and exports and enforcement of the narcotic law which were previously exercised by the Federal Narcotics Control Board and the Bureau of Internal Revenue, respectively. The Federal Narcotics Control Board was thereby abolished. The policy of the new Bureau was to cut off the supply of the illicit drug traffic at the source. Steps were taken to curb the smuggling of large quantities of contraband narcotics. At the same time the Bureau attacked the illicit domestic traffic.

The Law in Relation to the Addict: Among those apprehended in narcotic traffic, whether it be for possession or purveyance, the law recognizes no distinction between addict and non-addict. Judges, however, assert that they distinguish between the addict and the commercial supplier. They regard this distinction as fundamental in the application of penalty. They argue that the laws of penalty should have sufficient latitude to allow judicial discretion for imposing them on an individual basis. But, they complain, Congress has limited judicial power by enacting mandatory penalties.

In actuality, quite apart from the length of the sentence, there are no criteria, no system, no uniformity of practice in the disposition of arraigned addicts. Some are disposed of as criminals, some as sick persons. What happens to the arraigned addict seems to be a matter of unpredictable chance, perhaps largely depending upon the attitude and degree of enlightenment of the court.

The Law on Rehabilitation and Its Execution: Besides its enactment and enforcement of laws designed to limit the trade in narcotics to medical uses and thereby diminish the number of addicts, the Federal government has attempted to provide rehabilitation of the addicts through hospitalization in two Federal institutions. These hospitals in Fort Worth, Texas, and in Lexington, Kentucky, care for 1) those who, on conviction, are sentenced to confinement in such institutions, 2) those who are ordered to submit to such treatment as a condition of probation, and 3) patients who apply voluntarily for treatment. The statute authorizing the Surgeon-General to provide for the "care, protection, treatment, and discipline of" addicts commands: ". . . Such care and treatment shall be provided at hospitals of the Service especially equipped for the accommodation of such patients and shall be designed to rehabilitate such persons, to restore them to health, and where necessary, to train them to be self-supporting and self-reliant."

Of interest in the treatment of addicts is the confident and dogmatic pronouncement laid down in the Federal regulations. There it states: "It is well established that the ordinary case of addiction yields to proper treatment, and that addicts will remain permanently cured when drug taking is stopped and they are otherwise physically restored to health and strengthened in will power." In the Federal hospitals the addict is treated as a patient. Actual treatment begins with gradual withdrawal of the drug in order to break the addict's physical dependence on it. An important part of the treatment remains; for the problem contains a large psychological component.

Narcotic Laws and the Private Physician: Under the law, which was enacted for revenue purposes, the medical and allied professions are charged with the responsibility of prescribing narcotics under restrictions. Physicians may prescribe narcotics to patients for the relief of pain and discomfort associated with disease. They may attempt to treat an addict to free him of this habit, but only in a manner dictated by the Federal regulations. They may not prescribe a narcotic drug to keep comfortable a confirmed addict who refuses withdrawal but who might under regulated dosage lead a useful life and later might agree to withdrawal. These prohibitions are specifically set forth in the Federal regulations:

". . . This bureau has never sanctioned or approved the so-called reductive ambulatory treatment of addiction, however, for the reason that where the addict controls the dosage he will not be benefitted or cured."

"This bureau cannot under any circumstances sanction the treatment of mere addiction where the drugs are placed in the addict's possession, nor can it sanction the use of narcotics to cover a period in excess of thirty days, when personally administered by the physician to a patient either in a proper institution or unconfined. If a physician, pursuant to the so-called reductive ambulatory treatment, places narcotic drugs in the possession of the addict who is not confined, such action will be regarded as showing lack of good faith in the treatment of addiction and that the drugs were furnished to satisfy the cravings of the addict."

"An order purporting to be a prescription issued to an addict or habitual user of narcotics, not in the course of professional treatment in an attempted cure of the habit, but for the purpose of providing the user with narcotics sufficient to keep him comfortable by maintaining his customary use is not a prescription within the meaning and intent of the act; and the persons filling and receiving drugs under such an order, as well as the person issuing it, will be regarded as guilty of violation of the law."

It should be added that a verdict of guilty carries a prison sentence. All things considered it is small wonder that most physicians would prefer not to have addicts appear as patients in their offices.

Here is an instance where it would seem that control of medical practice has already come under Federal power. However incongruous it may seem, the government has achieved that control indirectly through a revenue measure.

It has been seen that the Federal government has attempted to minimize the spread of narcotic addiction through restrictions on the sale and use of narcotics and through suppressing illicit traffic in narcotics both internationally and domestically. It has exercised control over export and import of narcotics; particularly it has aimed to cut off illicit supply at its source and to curb smuggling. It has also exercised control over domestic traffic by regulating production, manufacture and distribution of narcotics. It has restricted the drug to medical and scientific use. Violations of the narcotic laws carry penalties. Under these laws the government has attempted to apprehend and sentence those engaged in illicit traffic. As has been noted, it achieves its objective indirectly.

These Federal regulations embody a philosophy of approach to the problem of drug addiction. First, it reflects the view that it is possible to stop the spread of drug addiction by prohibition of the drug. Deprivation of the drug is to be accomplished by stopping supply. Secondly, it reflects a punitive approach in that stiff penalties are to act as a deterrent. Thirdly, by virtue of possession or of selling the drugs, the drug addict is regarded as a criminal. Among violators of the narcotic laws no distinction is drawn between addicts and non-addicts. Fourthly, it exercises rigid control over the physician in the practice of medicine. It makes the physician responsible for administration of the drug; but it sets down medical opinions on prognosis and dictates the kind of treatment in statutes. The Harrison Act itself did not attempt to deal with the problems of the addict; it attempted only to regulate the flow of narcotic drugs. The interpretations of the Act, however, have altered what appears to have been the original intent of the measure in such a way that it is now difficult for physicians to render medical care to narcotic addicts except under carefully prescribed circumstances.

The Existing Situation

How effective has been this approach? Here we are actually concerned with its bearing upon two separate but interrelated components: traffic in narcotics and the drug addict. The latter in turn has two divisions: the formation of new addicts and the rehabilitation of existing addicts. First to be considered are narcotic traffic and the spread of addiction. Has there been diminution in the volume of traffic and spread of addiction? Is there proportionately more or less traffic and addiction prevalent? What is the existing situation?

Prevalence of Addiction and Illicit Traffic: There are assertions that there is an increased prevalence of drug addiction. If so, it may be inferred that there is an increase in drug traffic. But not all authorities accept this assertion. There are counter-claims that drug addiction under present regulations has diminished. The uncertainty grows out of a lack of substantiated and convincing statistics. There is no accurate information obtainable on the number of addicts in the country. Data on the number of arrests for violation of the narcotic laws do not give information on the number of undetected addicts in the nation; only those who come into contact with the law are now available for counting and even those do not provide an accurate measure of the prevalence of addiction because their arrests are too often recorded under other charges. A careful medical evaluation of those arrested as "thieves" would probably show that in a number of instances they should more properly have been classified as "addicts."

Inasmuch as the addicts are classed and hounded as criminals it is just about

as difficult to take a census of them as of burglars. Indeed, because of the nature of their violation it is more difficult, because burglaries, if not burglars, can be counted. Certainly it is not to be expected that drug addicts as presently persecuted are voluntarily going to step forth to be counted. Under our present statutes the addict makes every effort to avoid being among those counted in the statistics of the police and courts. Inasmuch as the present attitudes toward addicts are punitive rather than helpful and understanding, they have no desire to come into contact with those who will do no more than assure that they will no longer have access to their drug supply. So there is an abundance of estimates and opinions and a scarcity of hard facts. In the face of admittedly incomplete information it assuredly requires considerable boldness to maintain that drug addiction is on the wane. Indeed, according to an article in the press a few days ago, it was estimated by the Bureau of Narcotics that the proportion of addicts in the American population today is 3½ times what it was between 1938 and 1948.

What is more, there are strong indications that there has been a change in the type of addict which creates a situation that is even more sinister and ominous. Twenty years ago addicts were generally adults in the latter part of their life span; today addicts are predominantly under 30, not infrequently youths. A lifetime of addiction potentially lies ahead of them. The number of these young addicts multiplied by their life expectancy gives a numerical product that reveals today a situation of such magnitude that it far transcends that of two decades ago. Inasmuch as a considerable portion of these young addicts become "pushers," what with their long life expectancy in addiction, they have a correspondingly long period to engage in recruiting. The net effect is almost certain to be more vicious than an increased number of older addicts who can afford their habit.

Engaged in drug traffic are four grades of sellers:

1. The importer, rarely an addict, who "supervises" the smuggling of drugs by his employees and who arranges for their distribution to the wholesale outlet.
2. The professional wholesaler, also rarely an addict, who obtains his supply from a larger wholesaler or the importer, and who seldom has any contact with addicts.
3. The "peddler" who may be, but is not always, an addict, who sells directly to the "pusher" addicts in small amounts the supply he obtains from the wholesaler.
4. The "pusher," an addict who sells narcotic drugs to other addicts in order to obtain funds with which to purchase his own supply. By and large, the "pusher" does not deal in drugs in quantity. He is concerned with selling them to other addicts only in order to maintain his own supply, not to make a profit beyond his own financial needs.

This organization is sometimes called a drug ring.

For fundamentally the same reason, money, both the importer at the top and many "pusher" addicts are engaged in spreading addiction. But there the similarity ceases. For the importer's quest for money is to satisfy a desire for it in large quantities, which is potentially obtainable because of the big profits. For drug traffic is primarily an operation in economics. The narcotic laws shut off any legitimate source of drugs for a market with an uncontrollable craving. The stage is set for inflation with profits of such enormity as to strain the imagination. Prohibition of narcotics creates a situation in which traffic to supply the demand for a product legally unobtainable is highly hazardous but just as highly profitable. Because of the profit to be made in selling illicit drugs, attempts are made to attract new users. Drug rings constitute big business with all its aggressiveness to increase volume of sales. And what is more, a large part of the sales force are compulsive consumers of their own product without even a house discount.

The addict's search for money, unlike that of the importer, is to satisfy first and foremost a craving for drugs. In this respect the drug traffic has also undergone a change, largely in the kind of salesmen and customers. Previously the addict came to drugs in search of relief from pain, fatigue, or anxiety. He had his source of supply and the means to gratify his craving. He did not recruit new addicts. But today the young addict, with insufficient funds, is driven to "pushing" and creating new addicts in order to obtain a supply for his own needs.

Whereas the importer searches for new customers in order to increase the volume of sales because of the enormous profit to be gained, the "pusher" seeks new customers in order to increase his earnings so that he may be able to purchase the drug for which he has a craving that must be satisfied. His efforts to make new addicts may not even be voluntary. Sometimes, in order to maintain his habit, the addict who is a "pusher" is coerced into persuading non-users to try drugs in the hope that they will be "hooked" and become steady customers. From the standpoint of the importer, promotion of drugs and their greater acceptance among youth with the prospect of a life-time of repeat sales in this special consuming group, is a highly satisfactory and desirable enterprise. On the other hand, just as the young addict has potentially a longer span of addiction ahead of him, so he has a longer span of participating in drug traffic. So addiction and drug traffic increase each other successively in a vicious spiral.

If one were to rate the four levels of participants in drug traffic in terms of criminality and danger to society, the importer would rank first; the wholesaler, second; the peddler, third; and the "pusher," fourth. The most reprehensible of the drug suppliers is the one farthest removed from the drug users. The importers and wholesalers are clever criminals with great financial resources. They are most difficult to apprehend. To obtain their conviction requires careful preparation of their cases and ironclad evidence of law breaking. All this is a nearly impossible task. Certainly the hard-working staff presently attempting the impossible should not be criticized for not accomplishing it. Nor is there any strong reason to believe that a larger force would completely abolish illicit drug traffic. Indeed, the Commissioner of the Bureau of Narcotics was quoted in the press a few days ago as testifying that, "if you had the Army, the Navy, the Coast Guard, the F.B.I., the Customs Service and our [narcotics] service, you would not stop heroin coming through the Port of New York."

To combat and prevent addiction, the law depends on stiff penalties. The hazard of engaging in drug traffic is great because the penalty is high. But for the non-addict importer and wholesaler, the profits are correspondingly high. For the addict who "pushes" or peddles, the penalty and hazard are also great; but so is his craving for the drug. Indeed, the addict has so great a craving that he becomes determined to get the drug without counting the risk.

It has been noted that two types are engaged in drug traffic: the addict and the non-addict. The existing body of law does not draw a distinction between them in the application of penalties. To impose the severe penalties upon an addict who sells to other addicts or, out of fear, to non-addicts, is undesirable. Narcotic addicts should be considered sick persons and should not be penalized for activities which stem primarily from their ill-conceived attempts to alleviate their own suffering. As for those persons who are not drug addicts but who are interested only in their own personal gain without regard to the suffering and misery their commerce may cause, to impose severe penalties upon them is not only eminently just but highly desirable.

Drug Addiction and Crime: Drug addicts fall into the toils of the law in two ways: they are arrested for possession or sale of narcotics; or for hold-ups, house-

breaking, breaking into cars, shoplifting, prostitution, mugging, purse snatching, pickpocketry. Obviously their object in perpetrating these crimes is to obtain funds to meet their needs. Since drug addiction is characterized by a craving transcending all other appetites and since it is an extremely expensive habit, it may be presumed that it is the most pressing, though not necessarily the only, reason that the addict commits crime. Certainly a large volume of crime is associated with drug addiction. At present it is debated whether crime is a consequence or an antecedent of drug addiction. Perhaps both are true. There is not sufficient evidence to permit the ready conclusion that drug addiction is responsible for a large part or most of the crimes in the category of theft and larceny. It would be equally untrue to assert that all addicts, in addition to their violation of the narcotic laws, have criminal records. But it would not be beyond the realm of fair speculation to suggest that in a proportion of addicts the economics of their addiction led them to start or continue in crime.

Rehabilitation: Next to be considered is the record of success in attempted rehabilitation. Most of the treatment of addiction is conducted in the two Federal hospitals especially administered for that purpose. Although the private physician is allowed under the law to cure addicts if he follows the mode of treatment prescribed in the Federal regulations, for reasons which have already been brought out, as well as the difficulties inherent in attempting it on an outpatient basis, he seldom undertakes it. In the hospital actual treatment begins with gradual withdrawal of the drug. Failure of the jail system for addicts has proved useful in one respect. It shows conclusively that mere abstinence from narcotics for long periods of time does not cure addiction. A constructive approach to treatment must be based on something more than a mere separation from the drug supply. There is a large psychological element in drug addiction; hence measures to rectify it are a major part of the therapy.

When attempts are made to appraise the success of the therapeutic efforts, two difficulties are encountered: 1) obtaining reliable data; 2) setting standards. It is difficult to do any follow-up study on those addicts who are discharged from institutions providing treatment for them; for there is presently no way of keeping track of them other than by their voluntary communications. Hence, the records leave much to be desired as a basis for determining the period of time prior to relapse, whether the "cured" addict abstains from drugs one day, one month, one year or for life.

Even if the data were more reliable, it is disappointing, if not misleading, to apply the older and more conventional criterion; namely, the percentage of cures. One source reports that on the basis of five-year follow-ups the results at the U.S. Public Health Service Hospital in Lexington, Kentucky, were 20 per cent known abstinence; 35 per cent known relapse; 40 per cent not heard from or never contacted. It is pointed out that of the 40 per cent on whom data were not obtained, a considerable number may have continued to abstain since no hospital or police record of them could be found. Considering the success of treatment for drug addiction as a whole, another source states that: "Probably less than 50% of treated drug addicts remain free of their habit."

But addiction is not like a communicable disease in which one attack and subsequent recovery confers immunity for life. Actually it has a large psychological as well as physical component. Furthermore, it is related to so many characteristics of man that success in treatment is better expressed in a more relative term than "cure." Addicts do not constitute a homogeneous group. They vary in age, personality, constitution, environmental background, culture, their mode of becoming addicts, and the duration of their addiction, to name only a few points of

difference. Several broad groupings may be recognized. But to speak of the aggregate of addicts as a group, it must be borne in mind that the only thing they have in common is their addiction. These variables are reflected in the record of the effect of rehabilitative measures. In addition, the present state of knowledge on effective rehabilitation must be taken into account. Under these circumstances, it is misleading to speak of cures and to set a standard of freedom of addiction for the rest of the patient's life following an adequate period of therapy.

When effects of two years' therapy are judged by the length of abstinence before relapse the latest data show a wide range, with a small percentage having a long term abstinence. But successive subjection of relapsers to a regimen of rehabilitation brings each time a small but definite percentage of long term abstinence.

The explanation of these results is not entirely clear. There is very inadequate follow-up of discharged patients which assuredly must shorten the record of abstinences. Also of course the present medical approach to rehabilitation of the addict represents almost a first attempt with admittedly incomplete knowledge. Much remains to be learned about drug addiction and its causes which in turn will shed further light on treatment of it.

Examination of the record of success in rehabilitation is important for the light that it may shed on the biology of addiction and on the quality and quantity of rehabilitative efforts. Valid conclusions drawn from reliable data assist in answering significant questions about the biology of addiction and particularly its responsiveness to treatment. Does rehabilitation necessitate a simple or complex procedure? Is it a short or long process? Is the improvement temporary or permanent? From all available evidence it may be said with some confidence that addiction is a complex disease and may therefore require a complex therapeutic approach. Certainly with the presently available methods rehabilitation is a relatively long process. With a successive series of therapeutic courses the results show increasing improvement.

The answers to these questions are important in order to make policy and decisions on the approach to control of narcotic addiction. It may be fairly said that in the present state of knowledge rehabilitation does not offer a quick means to help stamp out existing addiction and prevent new recruits. But rehabilitation is an essential part of any program in controlling drug addiction. The urgent need is for additional knowledge and wider application.

In considering the quality and quantity of existing Federal rehabilitative services the following questions may properly be asked: Insofar as resources permit, is everything being done that should be done and is it being done well? Should the Federal institutions for rehabilitation of the drug addict be continued? Could these institutions do even more effective work with additional resources? Within the limitations of existing knowledge and their resources, it is our opinion that the quality of their services is beyond reproach. It is our belief, however, that there is insufficient use of these Federal institutions and that many more addicts should be undergoing treatment. This is of course a situation over which the institutions themselves have no control. Rather it points to inadequacies in the system of referrals or funds, or both.

In a sense the question whether the Federal institutions for the treatment of addicts should be continued is rhetorical. It is beyond dispute that there are existing addicts. This is cold reality, not an indefinite possibility. What is society going to do with or for them? Perhaps the most difficult part of the vast problem of drug addiction is the proposal of constructive steps for the care, supervision, and treatment of the existing addict.

There is valid reason to believe that these institutions could produce even more effective results in rehabilitation with additional resources. Under the present

system, rehabilitation ceases before it is finished. The addict, following his stay at the institution, is given carfare to his home and a warm farewell; then he is dumped as a solitary figure, penniless, very often friendless and without work, in a hostile society. It would test the mettle of a healthy man to undergo this experience; it must be a real trial to the discharged addict. Here is a gap that needs to be filled.

Conclusions on the Existing Situation

From this appraisal of developments under the present punitive approach to the problem of drug addiction, it is the Academy's belief that the following conclusions are justified:

The illicit drug traffic still persists and it prevails in an even more sinister form since it now enslaves many youths.

Twenty-five years of the present laws have not accomplished to an unequivocal extent: suppression of illicit drug traffic; prevention of the spread of drug addiction.

The punitive approach is no deterrent to the non-addict dealer or to the addict. The threat of stiff penalties in the form of jail sentences has not prevented the non-addict dealer or the addict from taking the risk. Furthermore, the serving of sentences in jail has not proved the solution of drug addiction. For one thing, the record of repeat jail sentences for addicts is so large that the procedure has been called "the revolving door policy." For another, confinement in jails succeeds in thoroughly instructing in the ways of the underworld those addicts who had not yet engaged in criminal activity. Particularly in the case of young addicts the jail sentence is a dangerous approach to a medical problem. During incarceration the young addict, who had perhaps not even finished school because of his subjection to narcotics, learns from other prisoners not a skill with which he can support himself, but how to get along without working at all, even less desirable ways of maintaining his drug habit, and a complete course in drug addiction. It has been demonstrated that a jail sentence does nothing to help the addict recover from his addiction.

In view of the enormously magnified economic aspects of drug traffic, perhaps the punitive approach may not be the most effective way to bring about substantial reduction in drug addiction.

Under the law, most of the addicts are regarded as criminals rather than sick persons.

The present Federal regulations control the practice of medicine in relation to drug addiction to such an extent, and so look upon the physician as a potential criminal, that he prefers not to include the treatment of drug addiction in his practice.

Drug addiction is a more serious and difficult social and medical problem when it affects youths than older persons.

Judged by the criteria of abstinence from narcotics and, of accession to a gainful occupation in society, the rehabilitation of the drug addict in our present state of knowledge is a highly expensive, exceedingly slow and prolonged procedure necessitating repetitive efforts.

As a means of stamping out drug addiction, prevention remains the most practical and essential step. The crux of any program aimed to rid society of drug addiction is to stop the formation of new addicts.

The program of the past has also been inadequate in two approaches which hold promise of contributing to the diminution of drug addiction: research and education.

The Payne Bill

The Payne Bill proposed amendments to the various narcotic laws bearing upon several aspects of the problem. Briefly stated, it would have transferred the Bureau of Narcotics from the Treasury Department to the Department of Justice; it would have expanded facilities for the care and rehabilitation of drug addicts; it would have instituted an education program in teacher training colleges; and it would have applied stiffer penalties for violation of the narcotic laws.

The proposed transfer of the Bureau of Narcotics from the Treasury Department to the Department of Justice was in accord with the recommendations of the Hoover Commission.

Contained in the preamble of the bill was this statement: ". . . the need continues and grows for reduction of the demand for such [narcotic] drugs through proper treatment, cure, and rehabilitation of persons already addicted to the use of narcotics." In accordance with this view, the Payne Bill proposed to provide suitable care and rehabilitation centers for those who were addicted to the use of narcotic drugs. Such treatment was to be under the jurisdiction of the Department of Health, Education and Welfare and included provisions for assistance to states establishing rehabilitation facilities as well as for the training of personnel to serve in such institutions.

The bill also proposed to encourage the establishment of training centers for teachers and in part to subsidize the compensation of instructors for such courses. Thus it provided for teachers and teacher training programs. Recognition of the need to train teachers to give narcotic education is also evidence that an adult education program would be desirable. These are healthy efforts toward prevention, especially in a long-range program. But they should not be expected to bring prophylactic results at once.

The Payne Bill continued the punitive approach with even stiffer penalties. For example, "Whoever sells, transfers, barters, exchanges, or gives away, or facilitates the sale, transfer, barter, exchange, or giving away, of any narcotic drug . . . to any person who has not attained the age of twenty-one years, shall, notwithstanding any other penalties provided by law, be punished by imprisonment for twenty years. For a second offense, . . . the offender shall suffer death, unless the jury qualifies its verdict by adding thereto 'without capital punishment', in which event he shall be sentenced to imprisonment for life." The giving of drugs without cost is presumed to take place in "hooking" a new addict. Both parties are frequently under twenty-one. The penalties of twenty years' imprisonment for the first offense and execution for the second, when applied to youths, seem slightly severe.

Furthermore, in inflicting extreme penalties for trafficking in illicit drugs, the proposed bill failed to recognize that narcotic addicts, even though engaging in activities designated by it as illegal, are first of all sick persons and only incidentally law breakers. At the very least, the measure should have provided for a careful review of each case by a competent medical board, to assure that the sale of narcotic drugs by an addict was not being perpetrated for profit alone.

The preamble of the bill stated that "strongly deterrent penal laws, with alert enforcement, are acknowledged to be the most effective method of terminating illicit traffic and supply of narcotic drugs for profit." The soundness and accuracy of this theory is open to question in practice. The spectre of the noble experiment in alcohol still hangs over us. Severe penalties apparently mean little or nothing when measured against potential profits or inner craving. The death penalty for addicts is said not to have stopped addiction in China.

The Academy's principal objections to the Payne Bill are its punitive approach

and excessive penalties. In its opinion, the bill would have been no more successful in stamping out addiction than the present laws which it would have amended. Indeed it might have brought an even greater degree of failure to the extent that its penalties were unreasonably excessive.

In short, the Payne Bill contained several commendable provisions, but these were more than offset by its continued punitive approach with fantastically severe penalties.

The Academy's Proposals

The objective is to stamp out drug addiction as completely as possible. The crux of this objective is to diminish the number of individuals becoming newly addicted. The natural decrease with time in the number of existing addicts must not be overbalanced by the formation of new addicts at a more rapid rate. Indeed, if the objective of little or no addiction is to be achieved, there must be little or no formation of new addicts. Furthermore, whatever the policy adopted to abolish new addiction, there still remains the responsibility for those presently addicted. Concurrently with the attempt to stop the formation of new addicts, efforts should be directed to rehabilitate as many presently addicted persons as is possible. As a second objective such efforts would not only reduce the prevalence but would also contribute to stopping the spread of addiction. Finally, medical supervision should be provided for individuals already addicted to narcotic drugs who are resistant to rehabilitation.

The Academy proposes a six-point program to achieve these objectives. It should be emphasized that all measures are to be instituted, not just one.

1. There should be a change in attitude toward the addict. He is a sick person, not a criminal. That he may commit criminal acts to maintain his drug supply is recognized; but it is unjust to consider him criminal simply because he uses narcotic drugs.

2. The Academy believes that the most effective way to eradicate drug addiction is to take the profit out of the illicit drug traffic. The causes of addiction are cited as: maladjustment; underprivilege; broken home; poverty. Such conditions may well be contributory factors, but they are not of themselves the prime cause. Rather, profit looms large as the principal factor.

In seeking ways to reduce the formation of new addicts, it is helpful to consider the mechanisms of addiction and its spread. Availability of the drug, ignorance, curiosity and persuasion are the necessary ingredients for initiating drug use. Curiosity and the need to conform to the behavioral code of his age-group is probably a factor in attracting an adolescent to the use of narcotic drugs. In this group, it is common practice to designate a non-user as "chicken" or as "a square" if he refuses to use drugs. For certain individuals the ridicule of his fellows is unbearable; even though not wishing to do so, he finds himself taking drugs and, ultimately an addict.

Prospective users are furnished drugs by the "pusher" until addiction occurs. But once this has taken place, the addict is required to pay for every dose and thus a life of slavery begins. Therefore, the formation of new addicts is principally the result of commercial exploitation. Contained in the preamble of the Payne Bill is the assertion: "Illicit traffic in narcotic drugs for profit are the primary and sustaining sources of addiction. . . .[sic]" If all profit were removed from dealings in narcotic drugs, there would be no incentive in giving away these drugs in an attempt to addict others.

The addict should be able to obtain his drugs at low cost under Federal control, in conjunction with efforts to have him undergo withdrawal. Under this plan, these

addicts, as sick persons, would apply for medical care and supervision. Criminal acts would no longer be necessary in order to obtain a supply of drugs and there would be no incentive to create new addicts. Agents and black markets would disappear from lack of patronage. Since about eighty-five per cent of the "pushers" on the streets are said to be addicts, they would be glad to forego this dangerous occupation if they were furnished with their needed drug. Thus the bulk of the traffic would substantially disappear. By its very nature this traffic requires many agents scattered in diffuse neighborhoods. If a few unaddicted "pushers" were all that remained to carry on the trade, they would present a lesser problem for apprehension by the police.

3. An integral part of the program would be medical supervision of existing addicts, with vigorous efforts toward their rehabilitation. No particular philosophy of stamping out drug addiction and traffic has an exclusive proprietary of rehabilitation. Whatever the method it must include a plan and operation to rehabilitate the existing addict. This objective carries three parts: 1) persuasion of the addict to undergo treatment and rehabilitation; 2) appraisal of the methods of treatment and their success; 3) supervision of addicts who were resistant to undergoing treatment or refractory to treatment.

By a change in social attitude which would regard them as sick persons, and by relieving them of the economic oppression of attempting to obtain their supply of drug at an exorbitant price, it will be possible to reach existing addicts in an orderly dignified way, not as probationed persons or sentenced criminals. They would come under supervision in the interest of health, not because of entanglement with the law. Thereafter, on a larger scale and in a humanitarian atmosphere, there would be opportunity to apply persuasion to undergo rehabilitation. It is reasonable to expect that more might accept the opportunity.

It is a temptation to think of addicts as a homogeneous group, whereas all that they have in common is their addiction. They differ in age, personality, constitution, social and cultural environment, and length of time of addiction. Each addict is therefore an individual therapeutic problem. Present methods to convert addicts into abstainers have comprised removal of the drug and then institution of rehabilitative measures. Physical dependence on drugs can be removed by the withdrawal treatment. The mental and emotional fixations, however, are to be overcome only through the individual's own efforts and desires. Psychotherapy cannot be forced upon him with any hope of lasting benefit. Rehabilitation of severely addicted individuals to the point where they abstain from drugs for the remainder of their lives has been shown to be an extremely slow process with an equally slow rate of success. The present therapeutic regimen has suffered from premature termination of support to the patient. There is a need to maintain continuing contact with recovered addicts so that they may be helped in resisting the return to use of a drug in stress situations. A counselling service for them is urgently needed.

Not all the addicts subscribing to the proposed plan will agree at once to undergo treatment. In accord with this concept that treatment of the addict must be individualistic, the Academy believes that in appropriate institutions it might be well to try a reverse order. After the addict has undergone education and rehabilitation and has obtained employment, there might be more success in inducing him to give up the drug. It has been asserted that many addicted individuals become enslaved between the ages of seventeen and twenty. It is evident that addiction then occurs before the individual has had an opportunity to acquire a skill by which he can earn an honest living. If he is furnished his drug in required amount, he may be willing to be trained in a useful trade. When he has been enabled to maintain his livelihood with his former fears and strains removed, he may be willing to give up drugs. Thus a change in social attitude and a different therapeutic approach

in appropriate instances might offer more success in persuading an addict to undergo treatment and in the results of that treatment.

Addicts resistant to undertaking therapy and continuously refractory to therapy, despite all efforts, should be supplied legally and cheaply with the minimum amount of their drug needs; and efforts to persuade them to undergo rehabilitation should be continued.

It is suggested therefore that there be developed a program whereby sufficient amounts of drugs can be legally and inexpensively supplied to addicts, while attempts are being made to have them undergo treatment. This service for narcotic addicts should be instituted in dispensary-clinics, preferably attached to hospitals, whether Federal, municipal or voluntary. No person should be given drugs at such a service clinic unless he is willing to enter a hospital for evaluation of his drug needs. After careful medical evaluation he should receive at cost from the service clinic the amount of drug which it has been medically determined that he requires.

The service clinic should be in operation twenty-four hours a day, seven days a week, to insure that no addict has the excuse that he could not obtain his supply from a legitimate source and was thus forced by his discomfort to seek his supply from illicit dispensers. At no time should he be given a supply of narcotics adequate for more than two days; if he is found to have sold or given away any of the supply to another person, he shall be liable to commitment to a hospital with attempted rehabilitation.

If an addict uses more than the amount of drug supplied to him for the prescribed period, he should not be penalized so long as he returns to the service clinic for his legitimate supply. But in the event of such a lapse from the pattern of his consumption of drugs, he should be re-admitted to the hospital for another evaluation of his drug needs.

Needless to say, all addicts receiving drugs from the service clinic or entering a hospital for evaluation and treatment should be photographed and fingerprinted; copies of such photographs and fingerprints should be sent to a central agency, while one copy is retained at the original clinic. By means of a punchcard system, monthly checks should be made by the central agency to insure that an addict is not obtaining supplies from more than one clinic. If such a violation is found to exist, the offending addict shall immediately be subject to commitment as a hospital patient.

It is visualized that such service clinics will be established all over the country. Thus it will be possible for an addict desiring to change his residence to transfer from one service clinic to another without encountering difficulties in maintaining his supply. Whenever an addict wishes to go to another community, he will notify his regular clinic of his intent. The clinic will in turn notify the central agency of his new location and will forward to the new clinic the record of his evaluation and his conduct at the original clinic.

Strictly enforced, these safeguards should eliminate any possibility of the use of the illicit market and should insure that only those with intractable addiction are actually receiving narcotics. It is also postulated that there will be no laxity in enforcing provisions for failure to abide by the service clinic regulations.

Much space, perhaps a disproportionate amount, has been devoted to detailing the provisions for furnishing drugs to the addicts who refuse treatment. Actually it is hoped that this group will be small in number and constantly diminishing. For, all the while, unrelenting attempts would be made to persuade the resistant addict to undergo therapy to break the habit.

It will be seen that this recommendation is a humane, reasonable, and promisingly effective method of distribution. It should be remembered that every addict will get his drug. Under the present laws to do that he must "push," rob, steal,

burglarize or commit forgery. For, he is desperate when he is without drugs.

This part of the program containing provision for distribution of drugs to addicts has been opposed on the basis of previous short-lived experience with drug clinics. Admittedly some of the clinics were abused; others had success. In any event, there was insufficient time for them to demonstrate their merits. There is an aura of mystery surrounding the peremptory and premature closing of them. From all available facts it would appear that they were closed, not because they had failed, but because operation of them did not accord with the prevailing philosophy of a punitive approach to a criminal problem.

4. It is proposed that there be no relaxation in the efforts toward complete and permanent elimination of the supply of illegal narcotic drugs and that provisions for suppression of illegal traffic be retained. It is the Academy's belief that the suggested plan to remove the profit would diminish illicit traffic. Whatever illicit operations were left after its application should be vigorously eradicated by appropriate laws, their enforcement, and provision for suitable penalties. Here illicit traffic should be re-defined to allow provision of drugs to addicts under medical supervision and treatment. This procedure should be surrounded by suitable safeguards. If anyone receiving drugs under the supportive plan should be found attempting to receive or to be receiving supplies from more than one clinic or from an illicit market, or if he be found attempting to sell or actually selling any of his supply to another person, he should be liable to commitment to a hospital with attempted rehabilitation. Thus he should be controlled as a sick person, not as a criminal.

Initially, it would be essential to provide the trained staff necessary to apprehend the peddlers, wholesalers and importers. It goes without saying that this group will not give up its lucrative business without a struggle. But a dearth of drug users, combined with severe penalties for dealing in narcotics, could be expected to put an end to the illicit drug traffic within a relatively short time.

It should be emphasized that the law should draw a distinction between the addict and non-addict in its provision. The convicted non-addict trafficker should feel its full force.

5. Adolescent addicts are reported to have said that they would not have taken drugs in the first place if they had known that they were going to become addicted. Such statements of youth are a strong argument for a good educational program for young people. The adult user, too, reports that he did not know the dangers of narcotic drugs when he began their use. If such reports are correct, it would appear that an educational program for adults as well as for adolescents is needed.

Combined with the medical care of narcotic addicts and severe penalties for trafficking in drugs, there should be an adequate program of education for adults, teachers and youth. By means of all education media, including radio, television, the public press, forum, lecture, books and pamphlets, there should be a concerted effort at informing the public of the dangers of narcotic drugs. Furthermore, there should be impressed upon the population the need to treat addicts, to apprehend illicit drug dealers, and to avoid the use of such drugs except under medical supervision.

6. One of the great difficulties in planning for a medical approach in the care and supervision of addicts is the lack of accurate information on their number. So long as they are stamped as criminals that difficulty will exist. It is a merit of the medical approach that by adopting the proper attitude toward them, it should be possible to study the epidemiology of drug addiction and acquire information about the magnitude and pathogenesis of the disease.

By means of the records accumulated at the central agency, it would be possible to have at all times an accurate count of the known resistant addicts in the country.

It would also be possible to know how many addicts were undergoing treatment for their illness and how many relapsed after a period of abstinence. Data on the length of abstinence from narcotic drugs and therefore on the success of various types of treatment would be obtainable. On the basis of such information, research could be focused more readily on the "why" of addiction and on improved methods of treatment. There seems little possibility of learning the "why" of addiction until narcotic addicts can be studied under conditions more nearly approximating normal existence than do those of a hospital, excellent though it may be.

So much has been stated about the relation of drug addiction and crime, particularly about the need for drugs leading to crime, that the Academy is moved to state that realistically it has no extravagant expectations that the proposed plan will completely eliminate crime. If a person was a criminal before he became a drug addict, it is not necessarily to be expected that he will cease to follow his predilections for crime just because he no longer is an addict. Perhaps it is fair to state that crime arising from the need for drugs may diminish; but criminal acts committed for other reasons may not decrease.

It is the opinion of the Academy that this program, taken in its entirety, is a reasonable and humane approach to the solution of drug addiction. It must be frankly admitted that there is no ideal or perfect solution. Of the two possible approaches to the solution of the problem, the punitive as against the medical, it becomes a matter of judgment as to which gives the more promise of effectiveness and contains fewer points of vulnerability. In judging between them the Academy believes that the evidence is preponderantly in favor of its proposed program as the more promising means of ridding the nation of drug addiction.

TWENTY-EIGHTH ANNUAL GRADUATE FORTNIGHT

THE NEW YORK ACADEMY OF MEDICINE

2 East 103 Street, New York

PROBLEMS OF AGING

OCTOBER 10–21, 1955

EVENING PROGRAM

First Week

Monday, October 10

OPENING ADDRESS
Edward J. Donovan, *President, The New York Academy of Medicine*

WHAT IS AGING? — *Ludwig Kast Lecture*
Albert Lansing, Emory University School of Medicine, Atlanta, Ga.

PSYCHOLOGIC ASPECTS OF AGING
Ross A. McFarland, Harvard University

EXPERIMENTAL PROLONGATION OF THE LIFE SPAN
Clive M. McCay, Cornell University, Ithaca, N. Y.

Tuesday, October 11

ARTHRITIS IN THE ELDERLY PATIENT
Joseph J. Bunim, National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland

THE EFFECT OF AGING ON THE MYOCARDIUM
William Dock, State University of New York College of Medicine at New York City, Brooklyn, N. Y.

FLUID AND ELECTROLYTE PROBLEMS IN SURGERY OF THE AGED
Henry T. Randall, Memorial Center for Cancer and Allied Diseases

RELATION OF INCREASED LONGEVITY TO NEOPLASIA
C. P. Rhoads, Memorial Center for Cancer and Allied Diseases

Wednesday, October 12

SOME PHYSIOLOGICAL ASPECTS OF AGING — *Wesley M. Carpenter Lecture*
N. W. Shock, National Heart Institute, Bethesda, Maryland

NUTRITIONAL PROBLEMS OF ADVANCING AGE
Fredrick J. Stare, Harvard University

GASTROINTESTINAL HEMORRHAGE IN ELDERLY PATIENTS
Thomas P. Almy, Cornell University Medical College

Thursday, October 13

PANEL MEETING — CEREBROVASCULAR DISEASE WITH AGING
Chairman: Irving S. Wright, Cornell University Medical College

Friday, October 14

PANEL MEETING — PROBLEMS OF RETIREMENT
Chairman: Howard Reid Craig, Director, The New York Academy of Medicine

(*Continued on next page*)

Second Week

Monday, October 17

THE NATURE OF THE RESPONSE TO STRESS WITH AGING — *Harlow Brooks Lecture*
James L. Whittenberger, Harvard University

EVALUATION AND PREPARATION OF THE PATIENT WITH DEGENERATIVE CARDIOVASCULAR DISEASE FOR MAJOR SURGERY
John S. La Due, The New York Hospital

THE AGING LUNG
Dickinson W. Richards, College of Physicians and Surgeons, Columbia University

Tuesday, October 18

MANAGEMENT OF INJURIES IN THE AGED
Robert H. Kennedy, Beekman-Downtown Hospital, New York

MANAGEMENT OF SURGICAL EMERGENCIES IN THE AGED
Condict W. Cutler, Jr., Goldwater Memorial Hospital, New York

SURGERY OF CHRONIC DISEASES IN THE AGED
Frank Glenn, The New York Hospital

ANESTHESIA IN THE AGED
Emanuel M. Papper, Presbyterian Hospital

Wednesday, October 19

EMOTIONAL AND PSYCHIATRIC PROBLEMS OF AGING
Francis J. Braceland, The Institute of Living, Hartford, Conn.

NEUROSURGICAL TREATMENT OF PARKINSONISM
Irving S. Cooper, New York University-Bellevue Medical Center

REHABILITATION IN THE AGED
Howard A. Rusk, New York University-Bellevue Medical Center

Thursday, October 20

PANEL MEETING — GONADAL FUNCTION AND INVOLUTION IN MAN — AND RELATED PRACTICAL MANAGEMENT
Chairman: Earl T. Engle, College of Physicians and Surgeons, Columbia University

Friday, October 21

PANEL MEETING — DISORDERS OF THE SPECIAL SENSE ORGANS ASSOCIATED WITH AGING: THEIR RECOGNITION AND TREATMENT
Chairman: Charles F. Wilkinson, Jr., New York University-Bellevue Medical Center

HOSPITAL CLINICS

Afternoon hospital clinics will be held at 19 of the metropolitan hospitals.

SCIENTIFIC EXHIBIT

A Scientific Exhibit will be on display throughout the Fortnight.

TWENTY-EIGHTH ANNUAL GRADUATE FORTNIGHT

MORNING PANEL PROGRAM

11:00 A.M. to 12:30 P.M.

First Week

Monday, October 10 — AGING AND ATHEROSCLEROSIS
Chairman: Henry S. Simms

Wednesday, October 12 — EVERYDAY PROBLEMS IN THE CARE OF THE AGED
Chairman: Frederic D. Zeman

Friday, October 14 — MANAGEMENT OF CARDIOVASCULAR RENAL PROBLEMS IN THE AGED
Chairman: Hugh Luckey

Second Week

Monday, October 17 — MANAGEMENT OF PROSTATIC OBSTRUCTION
Chairman: Robert S. Hotchkiss

Wednesday, October 19 — PUBLIC HEALTH ASPECTS OF AGING
Chairman: W. G. Smillie

Friday, October 21 — PROBLEMS OF INFECTIOUS DISEASES AND THEIR THERAPY IN THE AGED
Chairman: Perrin H. Long

REGISTRATION FEES

$10.00 for the entire program — $6.00 for either week.

Medical Officers of the Armed Services, in uniform, will be admitted without charge.

Interns and Residents will be admitted without charge, provided they present letters from their Chiefs of Service. They will be seated as facilities permit after Fellows of the Academy and other registrants have been accommodated.

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NOVEMBER 4, 1955 — **TOXIC EFFECTS OF THERAPEUTIC AGENTS**
Moderator: PAUL REZNIKOFF

DECEMBER 2, 1955 — **VALUE AND SCOPE OF ROUTINE ANNUAL PHYSICAL EXAMINATION**
Moderator: EDWARD P. CHILDS

JANUARY 6, 1956 — **MANAGEMENT OF SEVERE UPPER GASTROINTESTINAL HEMORRHAGE**
Moderator: FREDERICK H. AMENDOLA

FEBRUARY 3, 1956 — **THERAPY OF DISEASES OF THE GALLBLADDER AND BILE DUCTS**
Moderator: J. RUSSELL TWISS

MARCH 2, 1956 — **MANAGEMENT OF THE PAINFUL SHOULDER**
Moderator: HARRISON L. McLAUGHLIN

APRIL 6, 1956 — **SIGNIFICANCE AND MANAGEMENT OF "HEARTBURN"**
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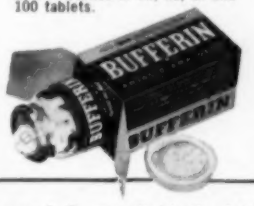

References: 1. Fremont-Smith, P.: J.A.M.A. 158:386, 1955. 2. J.A.M.A. 141:124, 1949. 3. M. Times 81:41, 1953.

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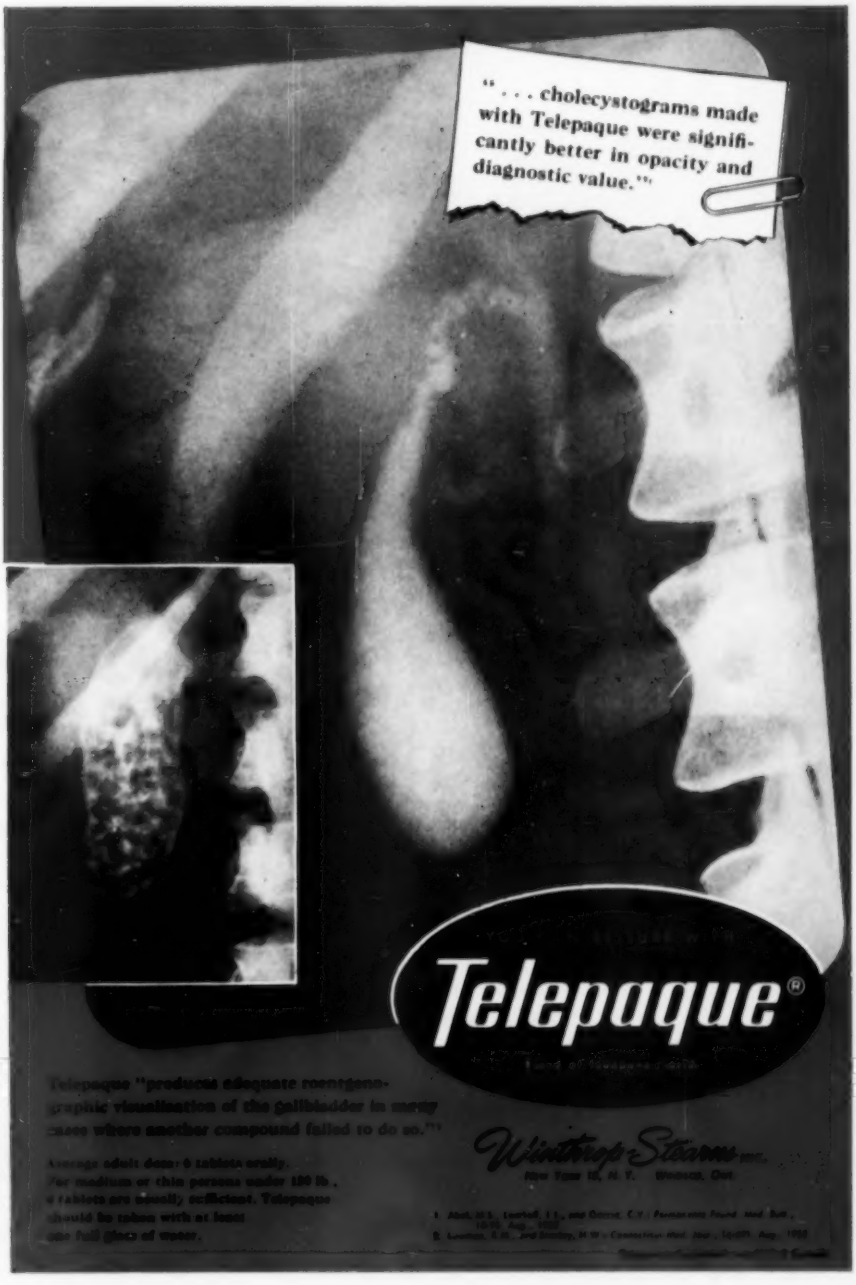
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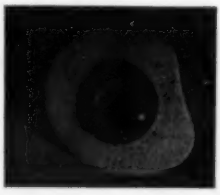

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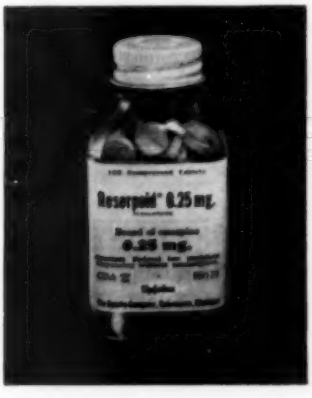

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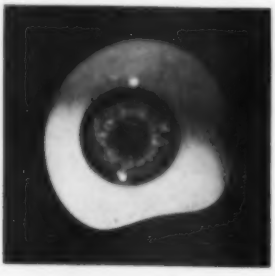

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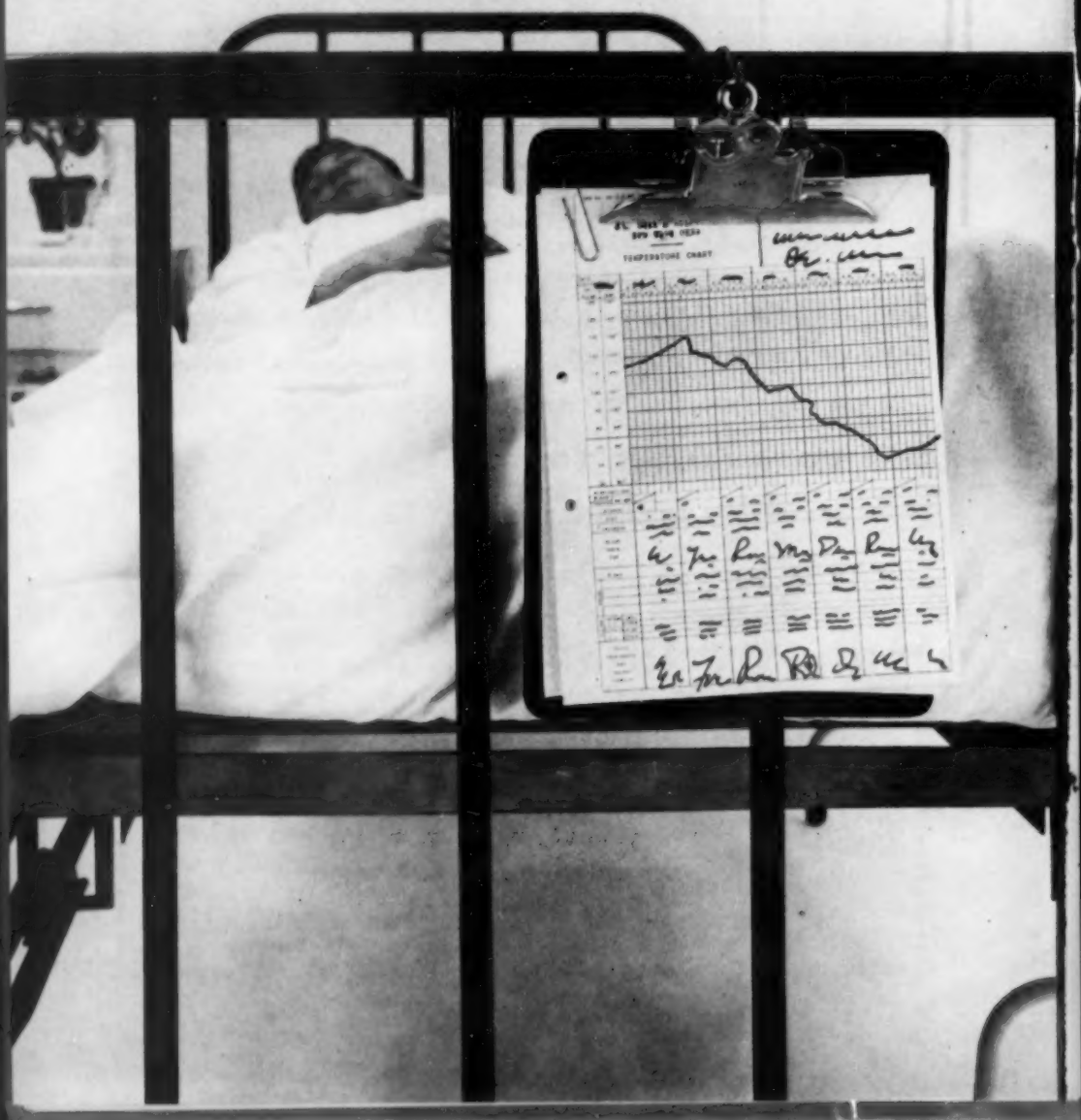

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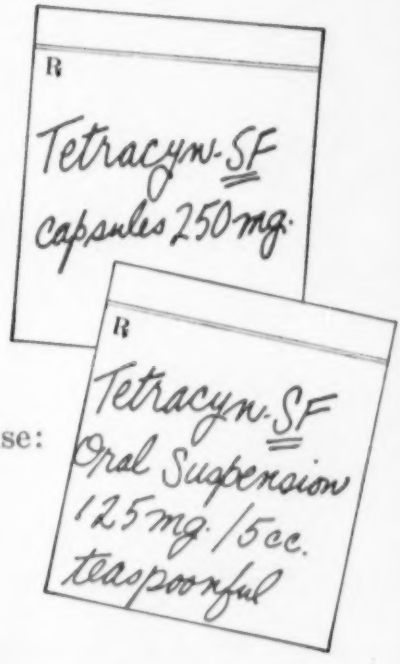

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1. Pollack, H., and Halpern, S. L.: Therapeutic Nutrition, Prepared in Collaboration with the Committee on Therapeutic Nutrition, Food and Nutrition Board, National Research Council, Washington, D. C., 1952. 2. Marti-Ibáñez, F.: Antibiotic Med. *1*:247 (May) 1955. 3. Dumas, K. J.; Carlozzi, M., and Wright, W. A.: Antibiotic Med. *1*:296 (May) 1955. 4. Milberg, M. B., and Michael, M., Jr.: Ann. New York Acad. Sc., In press. 5. Prigot, A.: Ibid.

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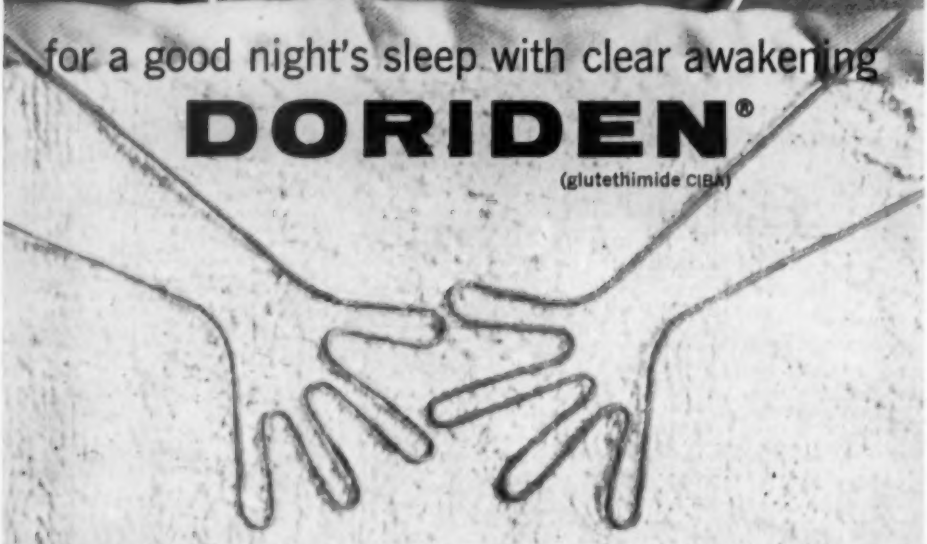

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